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Original Communications

PARAVERTEBRAL ALCOHOL BLOCK IN CARDIAC PAIN*

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SINCE the original suggestion of cervical sympathetectomy by François Franck and the first actual surgical interference for the relief of angina pectoris by Jonnesco of Bucharest in 1916, surgeons have attempted to relieve the agonizing pain incident to cardiovascular disturbance. That the surgical attempts are based on insufficient and inadequate anatomical, physiological and pathological evidence is amply borne out by the great variety of surgical procedures attempted.

The various surgical operations will be reviewed and discussed briefly, so that a clearer understanding may be obtained of the theoretical concepts upon which our own method is based.

1. *Method of Jonnesco:*[1] By this method the entire cervical chain, along with the first thoracic ganglion, was extirpated (Fig. 2). Danielopolu objected to this method. He contended that this operation severed the vasomotor fibers to the coronary arteries as well as the vasoconstrictor fibers to the lung. These objections were answered by Jonnesco[2] in a recent article. He asserted that physiologists, supported by extensive experimentation, are of the opinion that the sympathetics are not the vasodilators of the coronaries, but that on the contrary they are vasoconstrictors. Hence the removal of the sympathetics does not impair the efficiency of the coronaries but, in fact, augments it.

2. *Method of Danielopolu and Hristide:*[3] These operators sectioned the cervical sympathetic cord on the left side above the stellate ganglion (Fig. 3). Along with this section the spinal ganglia of the spinal nerves on the left side were injected with alcohol. They are not ready as yet to report the value of this method.

3. *Method of Danielopolu: A.* On January 1, 1924, this surgeon reported that Gino Pieri of Bellino was the first to follow the operator's new method. He sectioned the cervical sympathetic chain above the

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stellate ganglion, together with the vertebral nerve, as well as a nerve which joins the superior cervical ganglion to the cranial nerves (Fig. 4). The immediate results were good. No report as to the condition of the patient at a later date was given. *B.* In October, 1924, Danielopolu reported resection of the sympathetic cervical chain without removal of the inferior cervical ganglion and the first thoracic ganglion (Fig. 5). In addition he sectioned the vertebral nerve and the branches of the vagus, which were about to enter the thorax. *C.* In a less complete operation the superior and middle cervical ganglia are extirpated on one or both sides (Fig. 6). In January, 1925, Lilienthal[4] reported three such cases with good results. *D.* In February, 1925, the following operation was performed by Danielopolu: the cervical sympathetic chain was resected. The inferior cervical ganglia, as well as the first thoracic ganglia, were left intact. The vertebral nerve was sectioned. All branches leaving the vagus to enter the thorax were severed. The rami communicantes which joined the inferior cervical ganglion and the first thoracic ganglion to the last pair of cervical nerves were severed (Fig. 7).

In addition to the above operations Eppinger and Hofer sectioned the so-called depressor nerve, while Coffey and Brown[5] severed the cervical sympathetics, together with the superior cardiac nerve on the left side.

I have presented a review of the many surgical procedures with one purpose in mind; that is to emphasize the rebuke made by the late Sir James MacKenzie in a recent article in *The Lancet*.[6] He deplored the dangerous surgical interferences on such a meager anatomical, physiological and pathological foundation.

Recently Mandl[7] reported sixteen cases in which he injected novocaine, one-half of one per cent, paravertebrally. His results were excellent. The duration of the relief persisted for a long time and there were no deaths nor were there any severe unyielding complications. Luger[8] also reported one instance with excellent results based upon the above treatment.

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

Before reporting our procedure, a brief description of the cardioaortic afferent nervous system will be discussed. The method used is based upon the following anatomical and physiological facts. The cardiac plexus is brought into contact with the sympathetic system through three cardiac nerves, i.e., the superior, middle, and inferior cervical cardiac nerves. These nerves originate from the superior, middle, and inferior cervical ganglia. The right superior cervical cardiac nerve enters the deep cardiac plexus and gives a few branches to the anterior surface of the aorta. The left superior cervical cardiac nerve joins the superficial cardiac plexus. It is of importance to note that the superior cardiac nerve communicates freely with the middle cardiac nerve and with the superior cervical cardiac branch of the vagus. The middle

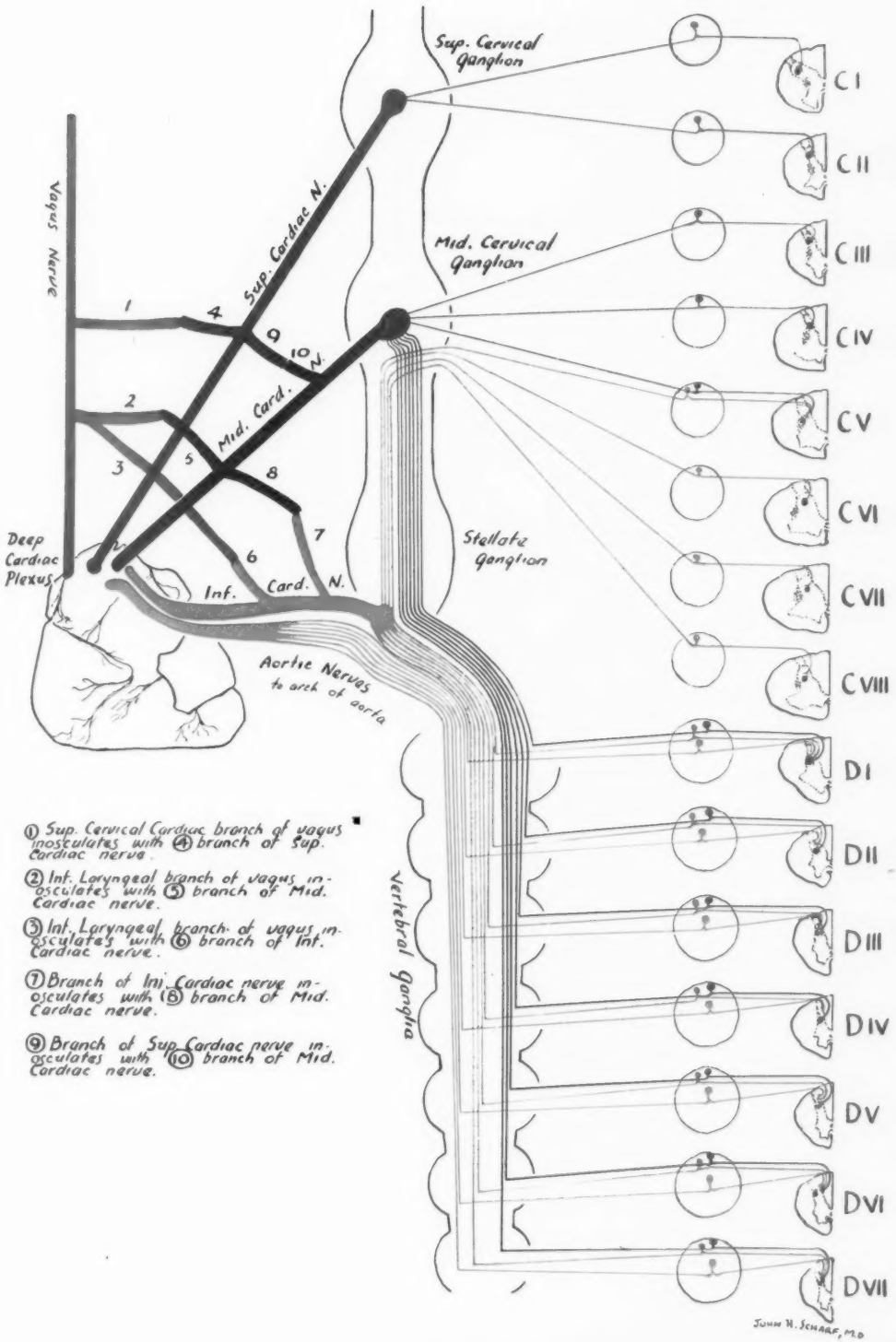
Sup. Cervical Ganglion
Mid. Cervical Ganglion
Stellate Ganglion
Vagus Nerve
Sup. Cardiac N.
Mid. Card.
Inf. Card. N.
Deep Cardiac Plexus
Aortic Nerves to arch of aorta
Vertebral Ganglia
1
2
3
4
5
6
7
8
9
10
C I
C II
C III
C IV
C V
C VI
C VII
C VIII
D I
D II
D III
D IV
D V
D VI
D VII
① Sup. Cervical Cardiac branch of vagus inosculates with ④ branch of Sup. Cardiac nerve.
② Inf. Laryngeal branch of vagus inosculates with ⑤ branch of Mid. Cardiac nerve.
③ Inf. Laryngeal branch of vagus inosculates with ⑥ branch of Inf. Cardiac nerve.
⑦ Branch of Inf. Cardiac nerve inosculates with ⑧ branch of Mid. Cardiac nerve.
⑨ Branch of Sup. Cardiac nerve inosculates with ⑩ branch of Mid. Cardiac nerve.
John H. Scharf, M.D.

Fig. 1.

cervical cardiac nerve arises from the middle cervical ganglia. Often this nerve and ganglion are entirely absent. Both the right and left middle cervical cardiac nerves end in the deep cardiac plexus. The middle cervical cardiac nerve inosculates in the neck with the superior cervical cardiac nerve and the inferior laryngeal nerve of the vagus.

The inferior cervical cardiac nerve arises from the inferior cervical ganglion and at times from the first thoracic ganglion. It inosculates with the middle cervical cardiac nerve and the inferior cardiac nerve. The lowest cardiac nerve terminates in the deep cardiac plexus. The

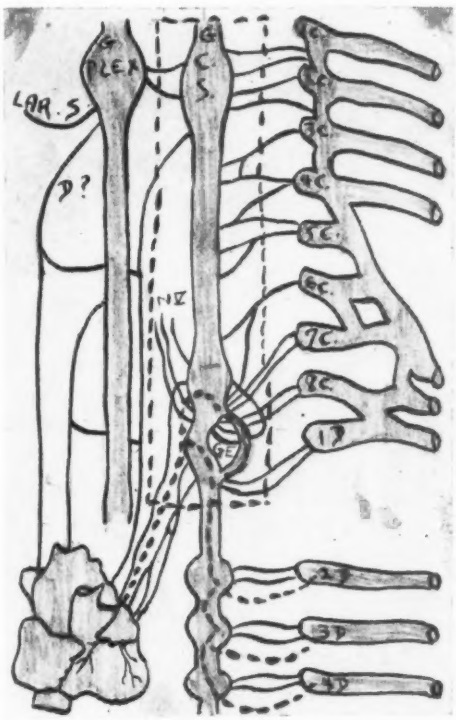

Fig. 2. (From Danielopolu.)

vagus nerve also ends in the deep cardiac plexus. The nerves of the heart are derived from the cardiac plexus. These nerves pass down along the aorta and are distributed to the auricles. From there they accompany the coronary arteries along the auriculoventricular groove, forming the coronary plexus. From this plexus branches are given off to the ventricles. The ascending aorta has nerve fibers which are in relationship, through the rami communicantes, with the first six spinal thoracic segments. There is some question as to whether the afferent fibers of the inferior cardiac nerve pass to the fourth, fifth, sixth and seventh cervical nerves. There is some evidence to the contrary. First, clinically, it is rare for pain to appear over the dermatomic segments

supplied by the fourth, fifth, sixth and seventh cervical roots. Embryologically there is also some evidence against this occurrence. Head[9] showed that afferent fibers from the heart enter the upper cervical and thoracic segments, extending from the first to the seventh dorsal segments. Apparently in the development the fibers going to the lower cervical nerves are not developed from the inferior cardiac nerves. All three cardiac nerves convey motor impulses to the cardiac plexus. Ranson[10] maintains that most or all of the constrictor fibers to the aorta and coronary vessels come through the superior cardiac nerve. The sensory afferent impulses from the middle and inferior cardiac nerves

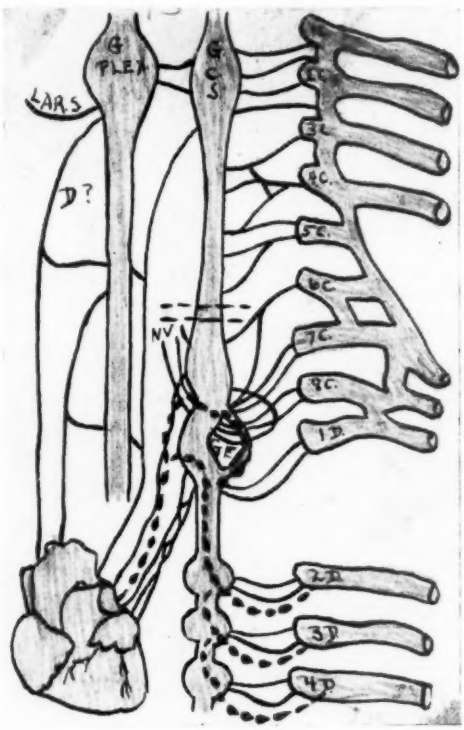

Fig. 3. (From Danielopolu.)

reach the spinal cord through the rami communicantes. They enter into the thoracic segments, extending from the first to the seventh segments.[11] These sensory afferent fibers are finely myelinated.[12] Edgeworth maintained that such fibers pass into the central nervous system by way of the rami communicantes into the upper thoracic segments.

The accompanying diagram (Fig. 1) is a representation of what is generally known and accepted concerning the anatomical and physiological connections of the cardiac nerves to the spinal cord. Hypothetical nerves, such as a special depressor nerve and the vertebral nerve and structures seen in comparative anatomical studies but not

established for human beings, have been passed over lightly in this discussion. Since every conceivable combination of operations has been performed and since the beneficial results are far from constant, an explanation of the varying results may be offered. A careful examination of the diagrammatic representation of the nervous mechanism shows quite conclusively that not only are the cervical ganglia in union with one another, but also that the cardiac nerves inosculate with each other as well as with fibers of the vagus. It is quite evident that the removal of any combination of ganglia and cardiac nerves leaves other pathways for pain stimuli to proceed to the brain stem and cord. Even

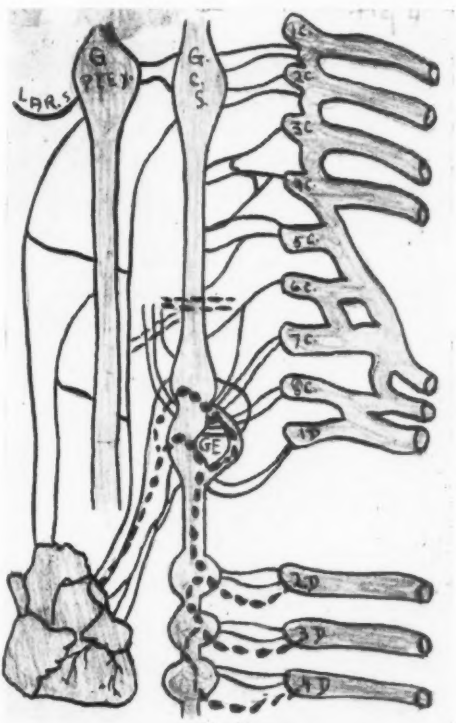

Fig. 4. (From Danielopolu.)

if one were bold enough to attempt in a human the extirpation of all of the cardiac nerves[13] on both sides, together with both vagi (if it were possible), impulses from the cardiac plexus and aorta would still pass into the spinal cord by means of the rami communicantes through the aortic nerves. They would enter into the cord from the first to the seventh dorsal segments.

Since most of the experimental work has been done on lower animals and since the operations on man have shown no definite constant results, the following question arises: What are the pathways for cardiac pain? At present the answer is not known. We do know, however,

that, irrespective of the place of origin of painful stimuli and irrespective of the cardiac nerves through which they pass, they must ultimately pass into the spinal cord or brain stem to travel by way of the spinothalamic tracts to the thalamus and ultimately reach the sphere of consciousness.

The problem can be solved by ascertaining definitely this point of entrance. With this knowledge, a mechanical interruption of the continuity of these entering fibers would prevent the pain stimuli from entering the cord. Head[14] and MacKenzie[15] suggested that painful

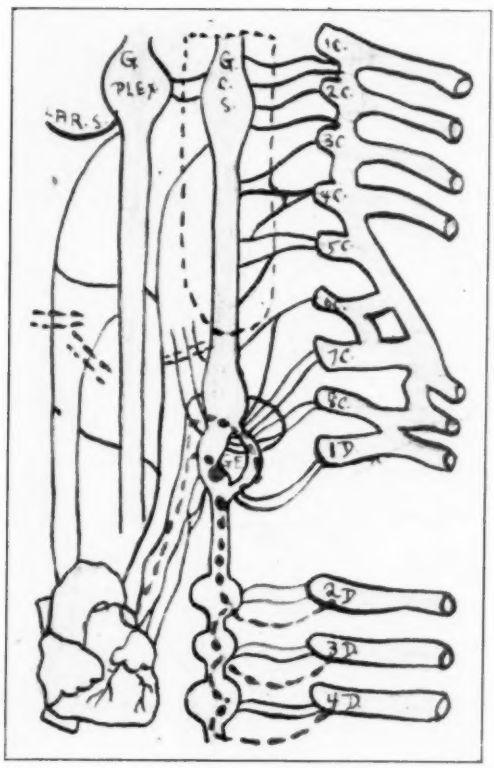

Fig. 5. (From Danielopolu.)

stimuli passed from the heart by means of sympathetic fibers to dorsal root ganglia; the pain was thus referred to the surface dermatomes supplied by the irritated dorsal root ganglia. Any method, therefore, that would indicate through which dorsal root ganglia the mass of pain stimuli are passing, would indicate the exact areas to which to apply surgical intervention in order to block this entrance of pain impulses into the spinal cord. Another neurophysiological conception is important. Cells in the dorsal root ganglia that are being bombarded are hyperirritable to external stimuli. If a dermatome supplied by an

irritable dorsal root ganglion is scratched with a pin or irritated by heat, it will produce a greater sensory reaction than would a skin area supplied by a normal dorsal root ganglion. Based on the foregoing premises, careful protopathic and epicritic sensory tests[16] are made to determine the dorsal root ganglia that are being bombarded by pain stimuli. The object, therefore, is to destroy the poorly myelinated afferent sensory fibers from the heart, which are passing through the sympathetic cords to enter a dorsal root ganglia. This can be done by destroying either the dorsal root ganglia or the afferent sensory, poorly myelinated fibers running in the sympathetic cords.

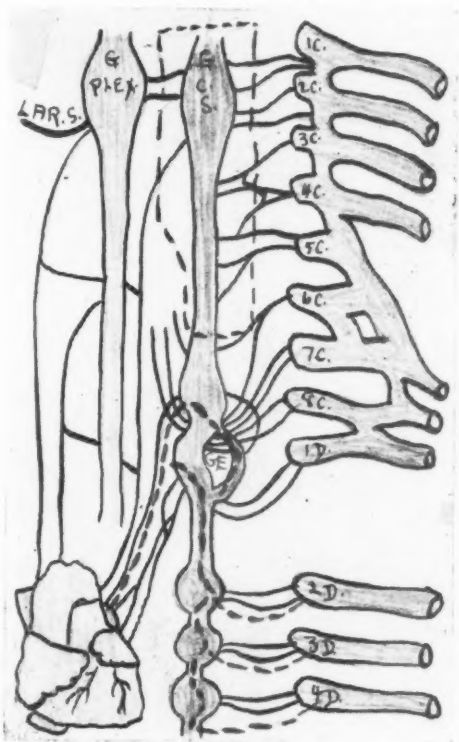

Fig. 6. (From Danielopolu.)

TECHNIC

A paravertebral injection is made and an eighty-five per cent solution of alcohol is introduced into or as near as possible to each dorsal root ganglion chosen. Five to eight cubic centimeters of the solution are used for each ganglion.

The technic is as follows: The patient is placed on the side opposite to the one to be injected. The knees are flexed on the thighs and the thighs on the abdomen and the head approximated to the lower extremities. Taking the twelfth rib as a landmark, the intercostal spaces to be injected are carefully palpated. A line is marked

on the skin through the midline of the vertebral spinous processes. At a point four centimeters from this line and over the ribs which are above the spaces to be injected, wheals of novocaine are raised. The wheals act both as a local anesthetic and as a landmark. The needle for the actual injection should be about eight centimeters long. The needle is introduced perpendicular to the posterior surface of the rib just above the space to be injected. As soon as the needle comes into contact with the rib, it is slightly withdrawn in order to change the direction. The shaft of the needle is directed downward, inward, and forward at an angle of 45 degrees. The point of the needle is advanced

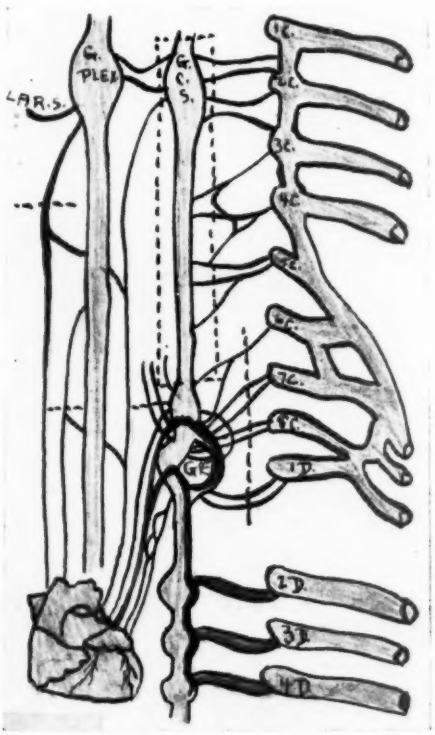

Fig. 7.

two centimeters further from the lower border of the rib. The point is then between the internal and external intercostal muscles. The needle is then attached to a water manometer[17] to determine whether or not it is in the pleural cavity. An absence of extensive oscillations synchronous with the respiratory movements of the chest indicates that the needle is not in the pleural cavity. This precaution is taken to obviate the possible injection of alcohol into the pleural cavity. The solution of alcohol is then introduced into each needle from a syringe. Half of the five cubic centimeters is injected without moving the needle, while the rest is distributed with a little to and fro movement as the

point is being withdrawn. The alcohol thus deposited produces an axonal degeneration of the thoracic nerve very near to the cell body. Some of the alcohol may even spread along to reach the intervertebral foramen and exert its action upon the ganglion itself.

CASE REPORTS

The first three cases are from the Medical Division, Montefiore Hospital, Service of Dr. B. S. Oppenheimer.

CASE I.—The patient, R. C., a young female, aged twenty years, suffered from aortitis and aortic insufficiency caused by congenital syphilis. Her complaints of pain began April, 1923. In the very beginning the pain appeared over the precordium. In a few months the discomfort extended to the left shoulder blade, down the left arm and the back of the chest on the left side. The arm pain was sticking and constricting in character and was especially bad during the night. After April 17, 1924 the pain became much more severe. The attacks consisted of paroxysms of severe sticking pains lasting a few minutes and leaving in their wake a dull ache over the same area. These paroxysms were brought on with only slight exercise, and, as a result, greatly curtailed her physical activities.

She received a course of salvarsan and mercury salicylate (which was completed October 2, 1924), potassium iodide (which was discontinued several months ago), and a series of injections of Bismogenol. Following this series of treatments she was slightly more comfortable, but the pain still persisted.

A paravertebral alcoholic injection was performed April 23, 1925. After the injection into the fourth, fifth, sixth, and seventh dorsal roots on the left side, the patient was almost completely relieved of pain and in addition was able to carry on increased physical activity to exhaustion without attacks of pain. For example, before the injection of alcohol she was unable to walk more than one block without developing sharp, excruciating, sticking pain over the left chest anteriorly and posteriorly, with radiation to the left arm as far down as the hand. The pain was so severe that she was forced to stop, the distress lasting two to three minutes at a time. At present she is able to walk from five to ten blocks, and, although she at times develops pain, she asserts that it is so mild and fleeting that she pays but little attention to it. Previous to the alcoholic injection she found that on attempting to practise on the piano for more than ten to fifteen minutes, she would be forced to stop because of the agonizing pain. Now she is able to play for at least one hour and at times more. Only occasionally has she a short fleeting pain over the left precordium. The following are the sensory changes observed before and after the injection.

April 22, 1925. *Before the injection* (Fig. 8).

A. Epicritic sensibilities.—(1) Hyperesthesia to light touch with cotton wool extended from the third to the seventh dorsal nerves on the left side anteriorly and posteriorly. (2) She was able to discriminate temperatures ranging between 20° and 38° C. over the same region. (3) Cutaneous localization was well performed.

B. Protopathic sensibilities.—(1) A zone of hyperalgesia to pin prick extended from the third to the seventh dorsal nerves on the left side. (2) A marked hyperthermalgesia was observed on the left side of the chest to temperatures above 45° and below 20° C., when compared to the right side. She was able to recognize these extreme differences in degrees on the left side.

June 1, 1925, thirty-nine days *after the injection.*

A. Epicritic sensibilities.—(1) A zone of hypesthesia to light touch with cotton wool extended from the third to the seventh dorsal nerves on the left side. In fact, she hardly perceived the stroke of the cotton wool. (2) She was definitely unable to discriminate over the injected segments, temperatures ranging from 26° to 38° C. (3) Cutaneous localization was greatly impaired.

B. Protopathic sensibilities.—(1) An area of hypalgesia to pin prick extended from the third to the seventh dorsal nerves on the left side. (2) A marked hypothermalgesia was found on the left side extending from the third to the seventh dorsal nerves, when compared with the right side. There was noticed great impairment in her ability to discriminate between extremes of temperature on the left side, i. e., between 20° and above 45° C.

Case Summary.—(1) Before injection a zone of dermatomic irritability extended from the third to the seventh dorsal nerves on the left side. Sensory examination thirty-nine days after the injection showed that the nerve conductivity was greatly reduced. (2) She had been free from pain for four months when she was dis-

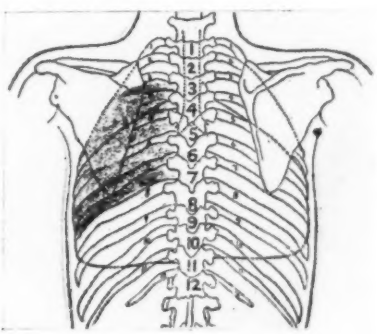

Fig. 8.

charged from the hospital. On October 25, 1925, approximately twenty-six weeks later, we received a letter from her in which she reported that she is able to walk as far as a mile without the appearance of pain.

Case II.—The patient, F. S., a male sixty-three years of age, suffered from angina pectoris, due to coronary disease. Fifteen months before admission he complained for the first time of a severe, boring, retrosternal pain which penetrated anteroposteriorly. Frequently he observed that the pain was burning in nature, simulating "a feeling of hot sand." At times it was so excruciating as to induce crying. The pain would persist for twenty to twenty-five minutes, requiring morphine for its control. He could walk no further than three blocks at a time, for, if he did, agonizing pain ensued. Twice this necessitated his being taken from the street to a hospital in an ambulance. Inhalation of amyl nitrite often relieved his attacks. Several months ago he felt for the first time slight burning paresthesia down the left upper extremity.

On June 25, 1925 he received a paravertebral injection of alcohol into the third, fourth, fifth, and seventh intercostal nerves on the left side. Five cubic centimeters of an eighty per cent alcohol solution were used in each dorsal root. Following this form of treatment the pains were completely relieved within twenty-four hours. There was practically no limit to his ability to walk. He was up and

about most of the day, doing errands in the hospital, and he definitely asserted that he was relieved of his pain. Nevertheless, shortness of breath, when he exerted himself unduly, was a very prominent symptom. A sensory examination was done before and after the injection.

June 23, 1925, *before the injection* (Fig. 9).

A. Epicritic sensibilities.—(1) A zone of hyperesthesia to light stroking with cotton wool was found over the skin supplied by the second to the eighth dorsal nerves on the left side both anteriorly and posteriorly. (2) No disturbance was observed in his ability to discriminate temperatures ranging between 20° and 38° C. He had no difficulty in locating areas lightly touched.

B. Protopathic sensibilities.—(1) An area of skin hyperalgesia to pin prick extended from the second to the eighth dorsal nerves on the left side. (2) An extreme hyperthermalgesia was present on the left side when compared with the right side. He was able to distinguish these extremes of temperature on the left side.

March 3, 1926, three hundred and thirteen days *after injection.*

A. Epicritic sensibilities.—(1) When stroked lightly with cotton wool over the dermatomic segments supplied by the injected nerves, the

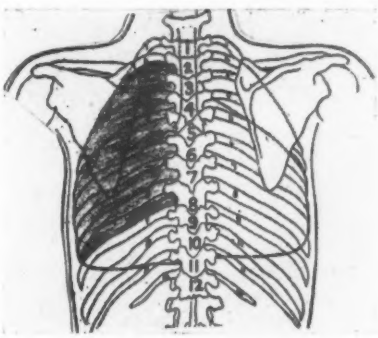

Fig. 9.

patient hardly perceived being touched. (2) He was unable to discriminate temperatures ranging between 20° and 38° C. (3) Cutaneous localization was completely lost.

B. Protopathic sensibilities.—(1) The patient observed that he could not feel the pricking of a pin over the areas of the skin supplied by the injected nerves. He experienced a peculiar dysesthesia, as he put it, "dull and frozen," when a pin was drawn across the skin. (2) His inability to discriminate the extremes of temperature was quite marked. There was, in fact, an almost complete analgesia.

Case Summary.—(1) Before injection, a dermatomic zone of irritability was delineated. This extended on the left side over the skin supplied by the second to the eighth dorsal nerves. Three hundred and thirteen days after the injection, a sensory examination indicated that the nerve conductivity was greatly decreased. (2) He was completely relieved of all pain for a period of four months when it again appeared. He was reinjected, this time blocking the first, second, third and fourth dorsal root ganglia and rami communicantes. Before the second injection the level of root hyperirritability was from the first to the third dorsal root segments. Following the injection signs of diminished conductivity were noted. He

is now again comfortable and free from all pain. He complains, however, of a pressing sensation over his shoulders when he attempts to rise from a sitting position, as well as of retrosternal pressure. He has now been relieved for a little more than ten months.

CASE III.—This patient, Y. S., a female, aged eighteen years, suffered from mitral stenosis and insufficiency, together with cardiac decompensation. Fifteen months before admission she developed precordial pain for the first time. She described it as sticking in character lasting from a few minutes to as long as an hour. At times the attacks of pain would appear during the night, awakening her from sleep. She complained that with the sticking pain there was a burning sensation in the skin. These attacks would appear for a few successive days and then disappear, only to reappear. For four months preceding the treatment, however, the pain had been persistent, always more or less severe. During the ten days before injection the agony was especially disturbing, being both sticking and constricting in type, with no remission either by day or night. The pain was particularly severe in the left interscapular region, preventing her from reclining on her back. On June 25, 1925, four cubic centimeters of a 60 per cent alcohol solution was injected into the third, fifth, seventh and ninth dorsal roots. After the injection she experienced precordial pain only occasionally and that which she did feel was slight and fleeting in character. She was able to recline on her back without pain or discomfort over the precordium. Within one week of the injection she observed a peculiar itching paresthesia over the site of the injection. On scratching it she noted that there was very little sensation induced on rubbing the skin.

The following is a summary of the sensory findings before and after the injection.

June 23, 1925, *before the injection* (Fig. 10).

A. Epicritic sensibilities.—(1) The dermatomic skin areas extending from the third to the eighth dorsal nerves on the left side both anteriorly and posteriorly showed a marked hyperesthesia. She noticed that light stroking with cotton wool induced an unpleasant scratching sensation. (2) Her ability to discriminate temperatures varying between 20° and 38° C. was normal. (3) Cutaneous localization was well performed.

B. Protopathic sensibilities.—(1) A dermatomic zone of hyperalgesia extended from the third to the eighth dorsal nerves on the left side. (2) In the same dermatomic zone hyperthermalgesia was observed when compared with the right side. Temperatures below 20° and above 45° C. were used. There was no disturbance in her ability to recognize extreme temperatures on the left side.

September 11, 1925, seventy-eight days *after the injection.*

A. Epicritic sensibilities.—(1) There was no disturbance in her ability to feel the light touch of cotton wool. (2) There was no disturbance in her ability to discriminate temperatures ranging between 20° and 30° C. (3) Cutaneous sensibility was found to be unimpaired.

B. Protopathic sensibilities.—(1) Her reaction to pin prick on the left side was only slightly below normal. (2) Her ability to discriminate on the left side between extremes of temperature, i. e., below 20° and above 45° C., was greatly impaired. When compared with the right side there was a definite hypothermalgesia.

Case Summary.—(1) This patient was injected with a weaker alcohol solution, i. e., 60 per cent. (2) The sensory findings after the injection showed the conductivity of the dorsal nerves to be only slightly decreased, as compared with the previous two cases in which an 80 per cent solution was injected. (3) She was free from all pain for fourteen weeks, finally dying from cardiac decompensation.

CASE IV.—The following patient is from the Neurological Division, Montefiore Hospital, Dr. S. P. Goodhart, Chief of Division.

The patient, J. W., a male, aged sixty-one years, suffering from angina pectoris associated with coronary disease and cerebral thrombosis, has for the past four years been complaining bitterly of precordial pain. At first the distress was brought on by walking two blocks, this causing such pain that he had to pause to rest. As time passed, he observed that walking even much shorter distances induced pain. He described this pain as sticking, tearing, and at times constricting in character. These attacks would appear two or three times daily, each lasting from twenty to thirty minutes. For the past eighteen months he has been unable to walk more than twenty yards because of the induced agony. Every morning at about two o'clock he was awakened by severe precordial pain persisting from thirty minutes to an hour. He sat up in bed grasping his precordium. Occasionally he had a fear of impending death.

On June 12, 1925, a paravertebral alcoholic injection was performed. A very interesting phenomenon occurred while the patient was on the operating table. He suddenly started to groan with pain which was localized to the precordium. Accompanying this excruciating agony he became cyanotic. While in the throes of this anguish, five cubic centimeters of 1 per cent novocaine solution were introduced

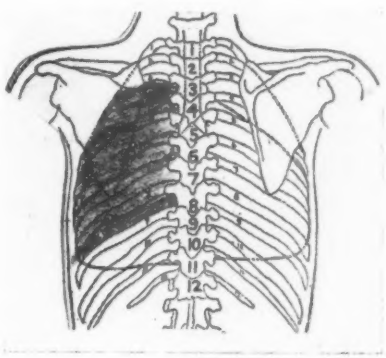

Fig. 10.

paravertebrally into the first and second dorsal nerves. Within thirty seconds pain had completely ceased. Five minutes later five cubic centimeters of an 80 per cent solution of alcohol were introduced into each of the two dorsal nerves. The next day he walked one hundred and fifty yards as fast as he could, and although he became alarmingly cyanotic and dyspneic, he asserted definitely that he had no pain. Since the treatment he has been able to walk about comfortably with almost complete absence of precordial pain. He has had no further attacks of nocturnal pain.

Sensory findings June 11, 1925. *Before the injection* (Fig. 11):

A. Epicritic sensibilities.—(1) A zone of hypesthesia extended over the entire left side of the chest both anteriorly and posteriorly. (2) He had great difficulty in discriminating differences in fine degrees of temperature on the left side, both anteriorly and posteriorly. (3) Cutaneous localization was definitely impaired over the entire left side.

B. Protopathic sensibilities.—(1) An area of hyperalgesia extended over the skin segments supplied by the first and second intercostal nerves on the left side. (2) A zone of hyperthermalgesia was observed on the left side over the first and second intercostal spaces. He found

no difficulty in discriminating between extremes of temperature over the hyperirritable zones.

Case Summary.—(1) Because of attacks of angina pectoris, the chest of a patient suffering from thrombotic processes, both in his interbrain as well as in the coronary arteries, was examined by sensory tests, which revealed disturbances in the afferent systems conveying impulses to the thalamus. Nevertheless, a zone of hyperalgesia was found over the skin areas supplied by the first and second intercostal nerves on the left side. (2) Because of signs pointing to a progression of the thrombotic process in his thalamus, it became quite evident that little information would be obtained by comparing the sensory examination of the chest before the injection with that after the injection. (3) No ill effects or complications of any kind following the injections have been observed. (4) He has now been relieved for approximately eight months.

Case V.—This patient, N. B., a male, aged sixty-five years, suffering from angina pectoris, due to coronary artery disease, has complained of pain over the heart for a period of two years. The pain was chiefly located over the precordium and radiated down the left upper extremity and was described as constricting in

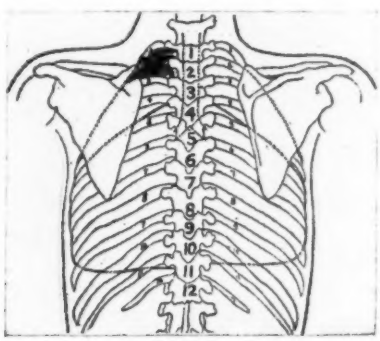

Fig. 11.

nature and at other times as sticking in type. Often the pain was boring, seeming to penetrate anteroposteriorly. The attacks often occurred two or three times daily. Almost every night about two o'clock he would be awakened by a terrific pain over the precordium, accompanied by a sense of suffocation and a fear of impending death. Venesection was resorted to several times. Morphia relieved him, but amyl nitrite was of little avail. Physical examination showed a greatly enlarged heart with a marked dilatation of the aorta.

A paravertebral injection of alcohol was made into the second, third, fourth and fifth dorsal roots, which relieved him of further attacks, both during the day as well as during the night. Shortness of breath still persisted upon exertion. Since the injection he has had several attacks of pulmonary edema with absence of pain. Before the treatment these attacks were always accompanied by severe, agonizing pain. Nine weeks later, during which time there was no pain, he suddenly died of pulmonary edema.

Sensory examination before and after injection showed the following:

September 15, 1925. *Before the injection* (Fig. 12).

A. Epicritic sensibilities.—(1) A zone of hyperesthesia to cotton wool was found over the skin supplied by the first to the sixth intercostal nerves on the left side. (2) There was no disturbance noted in his ability to discriminate temperatures ranging between 20° and 38° C. (3) Cutaneous localization was well performed.

B. Protopathic sensibilities.—(1) A zone of hyperalgesia extended over the skin supplied by the first to the sixth intercostal nerves on the left side. (2) There was noted a greatly increased reaction on the left side to temperatures below 20° and above 45° C. He had no difficulty in recognizing these extremes of temperature on the left side.

November 15, 1925. Sixty days *after the injection.*

A. Epicritic sensibilities.—(1) There was observed a marked hypesthesia which extended over the skin on the left side supplied by the first to the sixth intercostal nerves, respectively. In fact, he hardly perceived the stroking of the cotton wool over his skin. (2) He was completely unable to discriminate fine differences in temperature, i. e., between 20° and 38° C. (3) Cutaneous localization was greatly impaired.

B. Protopathic sensibilities.—(1) A zone of hypalgesia practically approaching analgesia extended over the skin segments supplied by the first to the sixth intercostal nerves. (2) A marked disturbance in his ability to discriminate between extremes of temperature, i. e., below

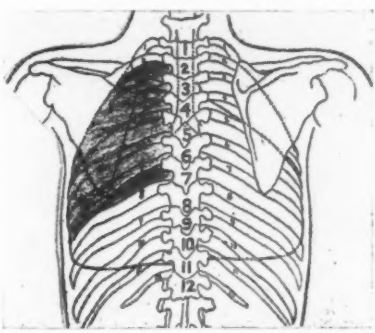

Fig. 12.

20° and above 45° C. on the left side was noted. When the affected area was compared with the right side a definite hypothermalgesia was noted to exist over the former.

Case Summary.—(1) Before the injection of alcohol a zone of hyperirritability existed over the skin dermatomes supplied by the first to the sixth intercostal nerves. Sixty-one days after the injection the conducting function of the intercostal nerves was greatly curtailed. (2) There was no return of pain in spite of the continuance of his attacks of pulmonary edema. On November 19, 1925, he died suddenly during one of these attacks. He was relieved for a period of nine weeks.

CASE VI.—Patient, W. H., male, aged seventy-two years, is suffering from angina pectoris due to coronary disease. He was first seen by me December 4, 1925. His attacks of pain began six or seven years before. He described the pain as vise-like and sticking in character. The pain would begin in the precordium and radiate down the left arm. Walking rapidly or going uphill would initiate the attacks of pain. During the last two years his condition became definitely worse. During the night he was forced to sit up in bed because of the sudden pain. These nocturnal attacks became so frequent that he would experience this extreme discomfort three and four times nightly. He would remain absolutely quiet and fixed during the attack and felt as though he were about to die. The

pain would last from fifteen minutes to an hour. For the past year his attacks would come on consistently after eating even light meals or after walking a half to one block.

Physical examination showed a moderately enlarged heart with a marked widening of the aorta. A soft systolic murmur was heard at the apex, which was transmitted to the axilla. The heart sounds were of poor quality.

A paravertebral alcoholic injection was made into the first, second, third, fourth and fifth dorsal ganglia. His course twelve weeks after the injection is as follows: He is able at present to walk twelve blocks without stopping, and there is no pain after this exertion. As was previously observed, the greatest distance he could walk before the injection was a half to one block. His appetite at present is excellent. Before the alcohol injection, the ingestion of even a little milk or cereal would initiate excruciating pain across the chest and down both arms. He would be forced to rise and stand absolutely at rest for as long as one hour before the attack would pass. At present he eats everything, meats, chicken, greasy foods, etc. He eats heartily and frequently with no pain. As a result of his increased diet, his general condition has improved. He has gained weight and his muscular tone, as evidenced by his quicker and firmer movements, has increased. The attacks, which occurred three to four times nightly have completely disappeared. Occasionally during the day he has a sharp, fleeting pain over the precordium. The blood pressure before the injection was systolic 145 mm. and diastolic 85 mm. At present the systolic pressure is 160 mm. and the diastolic 85 mm.

Sensory examination before and after the injection showed the following:

December 1, 1925. *Before the injection* (Fig. 13).

A. Epicritic sensibilities.—(1) A zone of hyperesthesia to cotton wool was found over the dermatomes supplied by the first to the fifth intercostal nerves on the left side. (2) There was observed no disturbance in his ability to differentiate fine gradations of temperature. (3) There was no disturbance in cutaneous localization.

B. Protopathic sensibilities.—(1) Hyperalgesic skin area was found to extend over the region supplied by the first to the fifth dorsal nerves on the left side. (2) There was present a marked hyperthermalgesia over the same areas as noted above, i. e., from first to fifth dorsal nerves.

February 28, 1926. Fifty-five days *after the injection.*

A. Epicritic sensibilities.—(1) A zone of anesthesia was found over the first to the fifth dermatomic segments posteriorly. Anteriorly, these segments showed a hypesthesia. (2) Fine differentiation of temperature was greatly impaired over the first to the fifth dermatomic segments. (3) Cutaneous localization was greatly impaired.

B. Protopathic sensibilities.—(1) A zone of analgesia was found to extend posteriorly over the skin segments supplied by the first to the fifth intercostal nerves. (2) A similar zone of diminished sensitiveness to extremes of temperature was noted over the same areas.

Case Summary.—(1) Before injection a zone of dermatomic irritability extended over the skin segments supplied by the first to the fifth dorsal nerves. Fifty-five days following the injection, signs of marked diminution of nerve conduction were observed. (2) Up to the date of this report, a period of twelve weeks, the patient suffering greatly from angina pectoris has been relieved of his pain. (3) The relief was accompanied by general physical improvement of the patient.

Case VII.—Patient, G. F., female, aged sixty years, suffered from angina pectoris secondary to extreme coronary disease. She was referred to us by her son-

in-law, a prominent physician in New York, who had observed her constantly for a long time. The following is a letter received from the doctor who gives the history briefly:

"The attacks of pain which Mrs. F. had were paroxysmal in character. The frequency of these attacks was variable, sometimes two and three times a day; towards the end they were almost continuous. The initial attack occurred about three years before, but at that time it was associated with hypertension and usually occurred upon exertion, particularly upon walking in the open.

"Physical examination at the time when you performed the operation was as follows: The heart was considerably enlarged, its action was variable, sometimes perfectly regular, at other times there appeared many extrasystoles. The musculature seemed poor and there were no adventitious sounds. The blood pressure varied between 130 and 140 mm. systolic and between 80 and 90 mm. diastolic. Originally the blood pressure was in excess of 200 mm.

"The condition at the time of exitus I cannot give you in detail. Following the operation the patient's attacks changed from painful to nonpainful ones and for twelve hours preceding exitus, her breathing was regular, heart action good, pulse full, rate about 100. The blood pressure was not taken. The exitus was sudden,

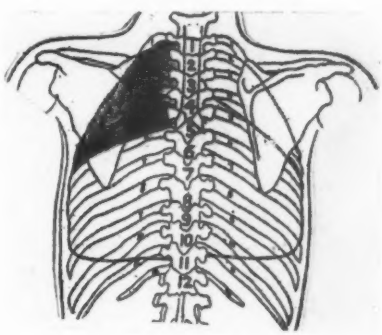

Fig. 13.

so that the desired observations were not made. Signs of pulmonary edema appeared in the last moments but death was cardiac in origin."

The condition of this patient before injection was extremely poor. She was in great distress from pain and required constant hypodermic injections of morphine. In fact, her condition was so poor, that the inadvisability of carrying out the therapeutic measure was seriously considered. The distress was so great, however, that the procedure was tried to give her her only chance for relief. For five days following the injection she had no pain. She could eat better and was able to recline flat on her back with only one pillow under her head, whereas before she required three to four pillows. Her color became good, and she was permitted to sit in a chair. On the sixth day she died suddenly. As observed by her physician, there was no pain during this sudden attack.

A preliminary sensory examination was done before the injection. (Fig. 14.) A zone of hyperirritability was found to extend over the skin supplied by the first to the ninth dorsal nerves on the left side. These nerves were blocked. Each root was injected with seven cubic centimeters of an 85 per cent solution of alcohol. Following the injection, sensory examination showed these roots to be destroyed, as they carried few peripheral sensory impulses.

Case Summary.—(1) An old woman, suffering from severe cardiac pain due to advanced coronary disease, was injected with alcohol paravertebrally. (2) Her

condition was so poor that the inadvisability of injecting was seriously considered. (3) Following the injection she was completely relieved of pain. During this period of freedom from pain she died suddenly.

CASE VIII.—This patient, M. A., male, aged sixty-two years, was first seen by me October 26, 1925. His complaints of pain over the precordium began approximately five years before. The pain was constricting in character and localized over the precordium and down the left arm. These attacks during the past five years were brought on by extreme exertion and were fleeting in character. As time went on the severity of the pain became markedly aggravated and the frequency increased to as many as two to three attacks daily. He used nitroglycerin constantly. In fact, he dared not move about without having the drug with him. Eight months before the injection, his condition became extremely aggravated. His repeated attacks during the day were severe and agonizing, persisting for ten or fifteen minutes and requiring nitroglycerin and absolute cessation of activities. During the night he was frequently awakened by these severe attacks. There was with each attack the fear of impending death.

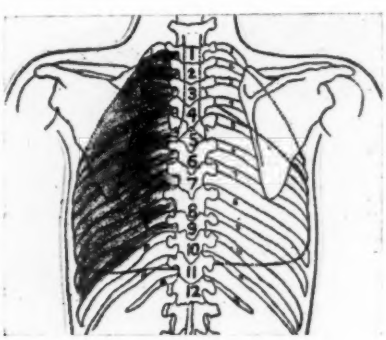

Fig. 14.

Physical examination showed an extremely enlarged heart and aorta. No adventitious sounds were heard. The heart sounds were faint and distant. His blood pressure was systolic 145 mm. and diastolic 80 mm.

On October 27, 1925 a paravertebral injection of alcohol was done on the left side. Seven cubic centimeters of an 85 per cent solution of alcohol were introduced into the first, second, third, fourth, fifth, sixth, seventh, eighth, and ninth dorsal nerves.

The following are the sensory findings observed before and after the injections:

October 26, 1925. *Before the injection* (Fig. 15).

A. Epicritic sensibilities.—(1) A zone of hyperesthesia to light touch with cotton wool extended over the skin segments supplied by the first to the ninth dorsal nerves, posteriorly and anteriorly. (2) Discriminating powers for temperatures ranging between 20° and 38° C. were intact. (3) Tactile localization was normal.

B. Protopathic sensibilities.—(1) A zone of hyperalgesia to pin prick extended on the left side of the skin segments supplied by the first to the ninth dorsal nerves. (2) A marked hyperthermalgesia was noted over the above corresponding skin segments. There was observed no abnormality in his ability to differentiate extremes of temperature.

March 1, 1926. One hundred and twenty-five days *after injection.*

A. Epicritic sensibilities.—(1) A zone of hypesthesia was observed to extend over the skin areas that previous to injection showed hyperesthesia. In fact, he hardly perceived the stroke of the cotton wool. (2) A marked hypothermesthesia was observed. He found great difficulty in differentiating fine degrees of temperature. (3) Cutaneous localization became greatly impaired.

B. Protopathic sensibilities.—(1) Instead of the previous hyperalgesia extending over the first to the ninth dermatomes, a marked hypalgesia almost approaching analgesia was observed. (2) His ability to feel extremes of temperature was greatly impaired.

Case Summary.—(1) Before injection a zone of dermatomic irritability extended from the first to the ninth dorsal nerves on the left side. Sensory examination, one hundred and twenty-five days after the injection showed that the nerve conductivity was greatly reduced. (2) His condition at present is as follows: (a) He requires no nitroglycerin. (b) The attacks of pain although still present are exceedingly mild and fleeting. Before injection they lasted ten to fifteen minutes, or as long as an hour, requiring large doses of nitroglycerin. The pains were so

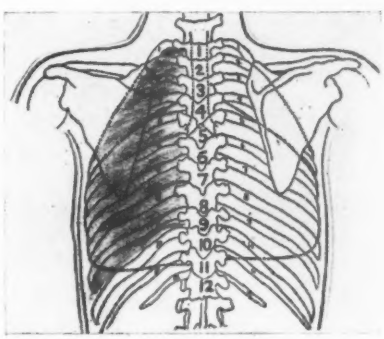

Fig. 15.

excruciating as to cause extreme anguish and fear of impending death. The pains now are very light and transitory, disappearing in a few seconds. There has been only one attack of pain during the night since the injection. His attacks of pain before injection alarmed his family exceedingly because of the general picture of extreme misery that he presented. Now the family is hardly aware that he has an attack of pain. He has now been comfortable for eighteen weeks.

DISCUSSION

In the brief review of the various surgical procedures, it is quite evident that the operators were and still are experimenting as to the pathway of pain. The variability of the nerve structures in the neck, the extensive inosculations between the vagus, superior, middle, and inferior cervical cardiac nerves, the numerous anomalies of structure, make it quite evident that inconstant results are to be expected from such surgical procedures. The fact that most of the impulses must enter the dorsal root ganglia before they can enter the spinal cord, suggests a different site for therapeutic procedures. Since the pain stimuli

from the heart must enter the spinal cord via the dorsal root ganglia, an irritation of the small cells in the ganglia is set up. The irritation of these cells in the dorsal root ganglia causes them to be more sensitive to external stimuli. Therefore peripheral irritation of the dermatomes supplied by these dorsal ganglia will show greater sensitiveness. Since these pain-bearing fibers, which are peripheral arms of the small cells in the dorsal root ganglia, are poorly myelinated, they are easily destroyed by alcohol, probably producing a wallerian degeneration. These fibers run in the rami communicantes to enter the spinal cord via the dorsal root ganglia.

SUMMARY

In a group of eight cardiac patients suffering from attacks of severe precordial pain, who were treated by paravertebral alcohol injections of the dorsal root ganglia, prompt and satisfactory relief from pain was secured in every instance.

The freedom from pain following a single injection has usually lasted several months. In one patient, who was reinjected after four months of relief, there has been a second period of comfort lasting several months.

No complications were encountered and no serious after-effects were seen.

The procedure is simple and is based upon definite neurophysiological facts.

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A CASE OF VENTRICULAR TACHYCARDIA AND AURICULAR FIBRILLATION: AN UNUSUAL PROBLEM IN THERAPY*

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THE details of this patient's illness are reported because of the unusual features that were found and because of the peculiar therapeutic problems that arose. As will be evident below, it seemed at first that we were dealing with a simple case of auricular fibrillation in a man who had mitral stenosis. On more careful study, and only when the electrocardiograms were correctly interpreted, it became clear that, although the auricles were fibrillating, practically all of the ventrical contractions were the result of ectopic ventricular beats (Fig. 1) and proper therapy became a difficult matter. There were two independent mechanisms involved in the disorder. It was considered that there were two circus movements occurring in the heart simultaneously. It is now generally accepted that auricular fibrillation is due to such a circus motion and it is not unlikely that the same is true of ventricular tachycardia. At least, the latter condition illustrates certain features that have recently called the attention of some observers to this possibility.

When the patient was first seen, he was put on the customary course of treatment for one with signs of failing circulation. A complete course of digitalis was given, but the heart rate did not change particularly for the ventricular tachycardia was uninfluenced (Fig. 2). This is just as one would have expected for, although auriculoventricular conduction could be impaired by digitalis, no appreciable slowing of the ventricular rate could occur because only a few beats were reaching the ventricles from the auricles even before treatment was started. It, therefore, was primarily necessary to inhibit the independent ventricular beats in order to reduce the condition to a simple problem of auricular fibrillation and then to treat that condition in the ordinary way. There was no other therapeutic agent available for this than quinidine which might either stop the ventricular tachycardia, the auricular fibrillation, or both. The patient was, therefore, given increasing doses of quinidine sulphate. At this time his condition was very grave. He had Cheyne-Stokes' breathing and it seemed that, if the rapid ventricular rate remained unchecked, he would die. As the dose of quinidine increased, the ventricular rate slowed (Fig. 3). The rapidity of both the ventricular tachycardia and the supraventricular beats was affected (Fig. 4), the former as a direct effect of the quinidine and the latter as a result of the previous digitalis. When the dose of 0.8 gm. of quinidine was reached, the mech-

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anism of the heart suddenly changed and it was found that both the auricles and the ventricles were contracting regularly (Fig. 5). He quickly improved and a few weeks later was discharged from the hospital as an ambulatory patient.

Having once regularized the heart with quinidine, the problem was to keep it so. This was found to be difficult because, on what was consid-

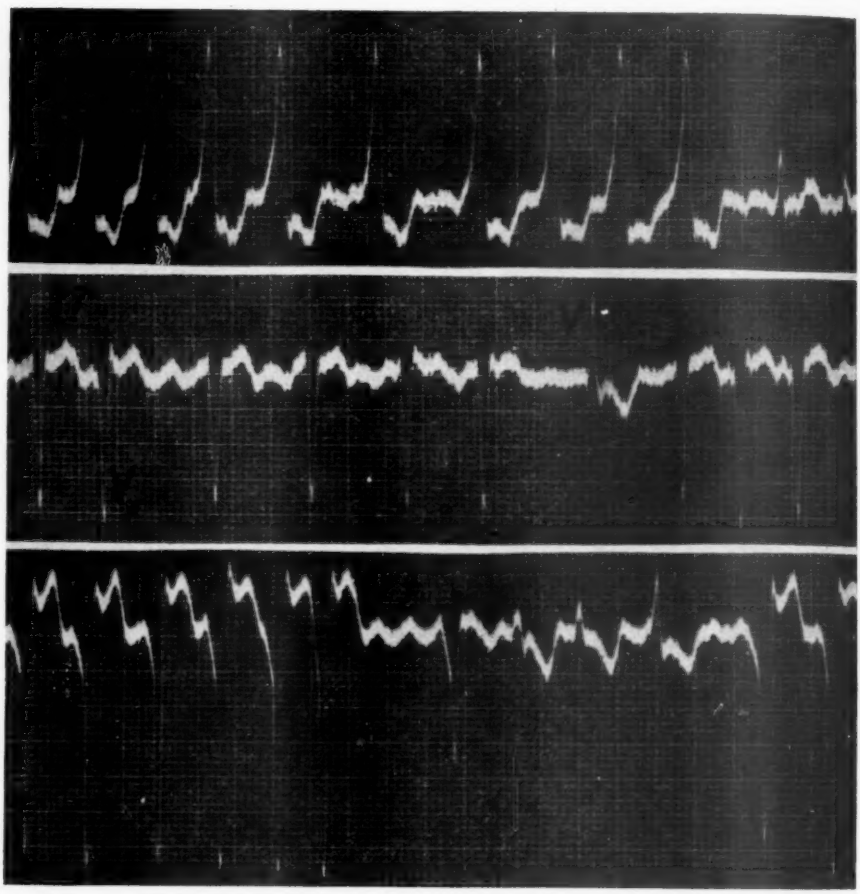

Fig. 1.—May 27, 1925. Three leads showing auricular fibrillation (f-f-f) and ventricular tachycardia (Vx). Note the occasional supraventricular beats (v). Rate 144.

ered to be large doses of the drug, ventricular tachycardia had a tendency to return (Figs. 6 and 7). Various combinations of quinidine with and without digitalis were tried (Table I). For a while, it was thought that some digitalis was necessary because it was found, on occasions, that the ventricular tachycardia was absent, but the heart rate was still rapid merely as a result of the auricular fibrillation (Figs. 8 and 9). No matter what the cause of the rapidity, an embarrassed cir-

TABLE I

DETAILS OF THERAPY

DATE*	MEDICATION§	HEART RATE	ELECTROCARDIOGRAMS	FIG. NO.	VITAL CAPACITY C.C.
5-30-25	None for one week	Irregular 144	Auricular fibrillation and ventricular tachycardia.	1.	1500 34%
6-11-25	Digitalis 2.7 gm.	Irregular 183	Auricular fibrillation and ventricular tachycardia.	2.	2300
6-16-25	Quinidine 5.8 gm.	Irregular 99	Auricular fibrillation and ventricular tachycardia.	4.	1900
6-17-25	Quinidine 2.1 gm.	Regular 73	Normal rhythm.	–	–
6-19-25	Quinidine 2.3 gm.	Regular 65	Normal rhythm.	5.	2700
7- 1-25	Quinidine 7.3 gm.	Irregular 141	Auricular fibrillation and short runs of vent. tachy.	–	2800
7- 6-25	Quinidine 6.9 gm.	Regular 80	Normal rhythm.	–	2400
7- 9-25	Quinidine 3.0 gm.	Irregular 150	Auricular fibrillation and ventricular tachycardia.	6.	–
7-16-25	Quinidine 12.1 gm.	Regular 75	Normal rhythm.	7.	2900
7-31-25	Quinidine 27.0 gm.	Irregular 148	Impure auricular flutter.	9.	–
8-14-25	Quinidine 16.8 gm. Digitalis 2.8 gm.	Regular 85	Normal rhythm.	10.	–
8-28-25	Digitalis 2.3 gm.	Irregular 162	Auricular fibrillation and ventricular tachycardia.	–	2200
9-11-25	Quinidine 16.8 gm. Digitalis 2.3 gm.	Regular 85	Normal rhythm.	–	–
9-27-25	Quinidine 15.6 gm. Digitalis 1.3 gm.	Irregular 130	Auricular fibrillation and ventricular tachycardia.	–	2300
10- 9-25	Quinidine 14.4 gm.	Regular 84	Normal rhythm.	–	–
10-25-25	Quinidine 19.2 gm.	Regular 125	?Auricular fibrillation and ventricular tachycardia.	11.	–
11-13-25	Quinidine 21.0 gm. (None for last 5 days)	Irregular 150	Auricular fibrillation and ventricular tachycardia.	–	2200
11-16-25	Quinidine 3.0 gm.	Regular 85	Normal rhythm.	–	–

From this date up to the present, March 28, 1926, patient has been taking 0.8 gm. of quinidine three times a day and the heart has remained constantly regular and he has been steadily at work.

*Date of electrocardiogram.

§Drugs given during interval between previous and present tracing.

culation would result and for this reason it seemed wise to give digitalis. A further difficulty arose in interpreting the prevailing mechanism of the heart, as is indicated by Fig. 10. At this time, the heart was found to be regular and rapid, but the mechanism was due to ventricular tachycardia and the auricles were probably still fibrillating.

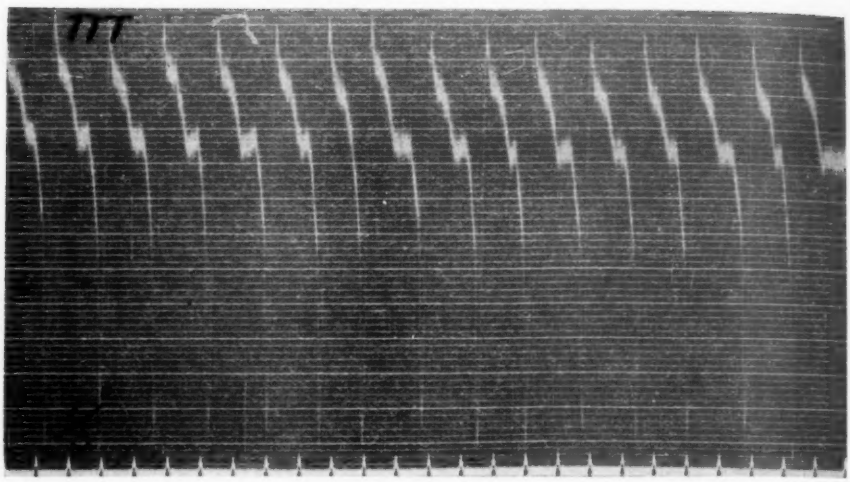

Fig. 2.—June 11, 1925. Lead 3. Rapid ventricular tachycardia. Rate 183. Note absence of supraventricular beats and increased rate as a result of digitalis.

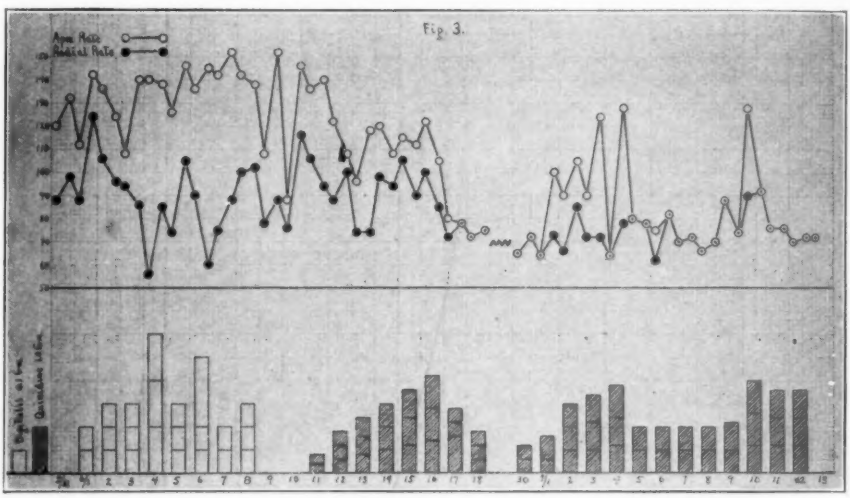

Fig. 3.

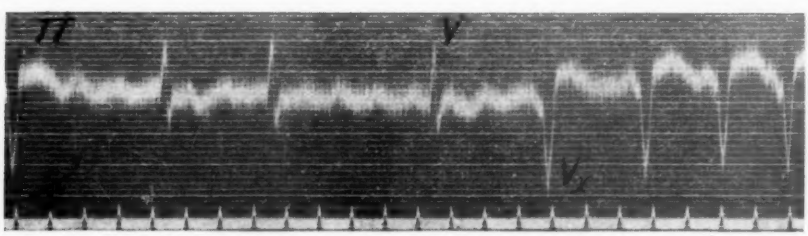

Fig. 4.—June 16, 1925. Lead 2. Note slowing effect of quinidine on the ventricular tachycardia (Vx). The supraventricular beats (V) are also slowed, probably as a result of the previous digitalis.

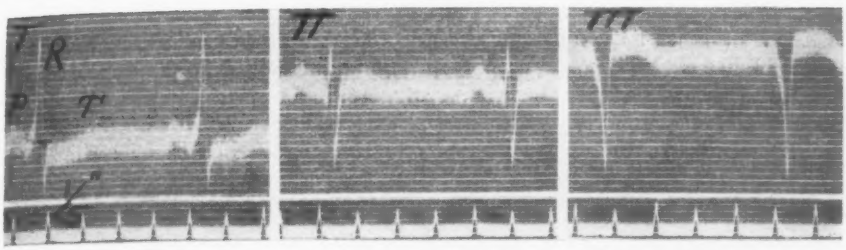

Fig. 5.—June 19, 1925. Three leads showing a normal heart mechanism.

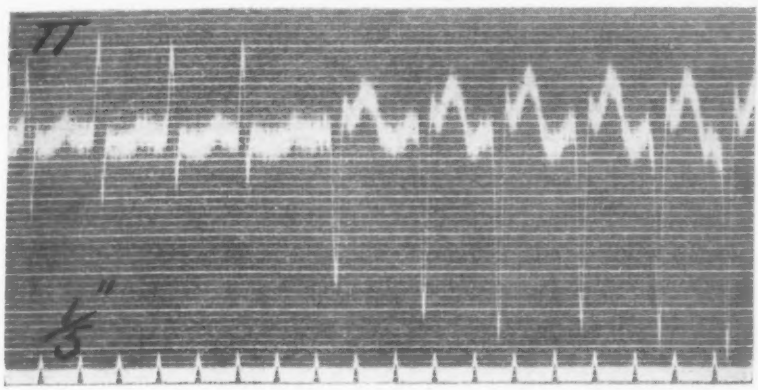

Fig. 6.—July 9, 1925. Lead 2. Note the return of the ventricular tachycardia on 0.5 gm. quinidine twice daily.

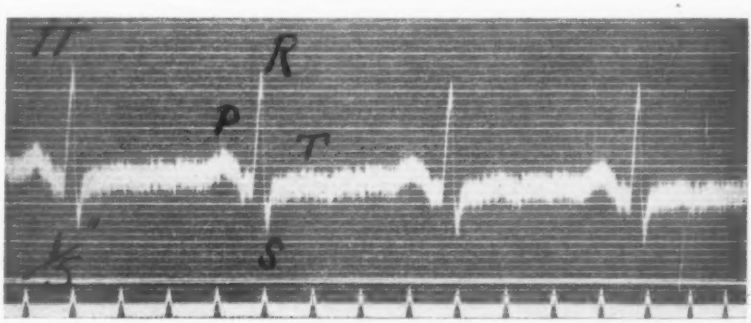

Fig. 7.—July 16, 1925. Lead 2. Return to regular rhythm on increasing doses of quinidine.

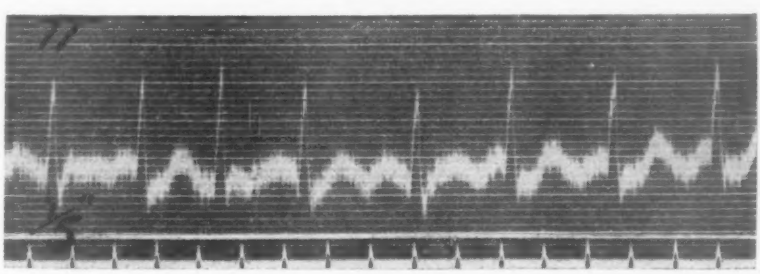

Fig. 8.—July 31, 1925. Lead 2. Impure auricular flutter, without ventricular tachycardia, developing on 0.6 gm. quinidine three times a day.

Finally, it was decided that, as a result of the various experiences with different doses of quinidine, none but maximum doses could prevent a return of the ventricular tachycardia. The patient was, therefore, given

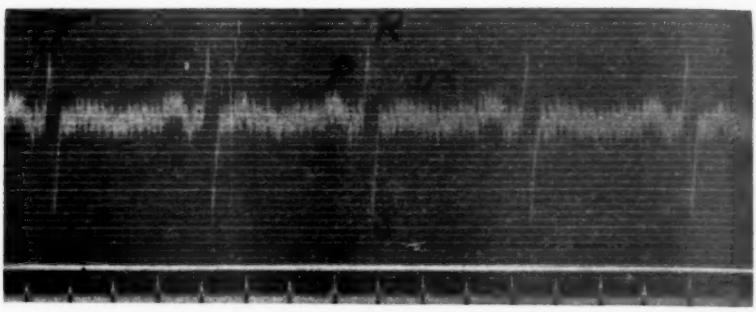

Fig. 9.—August 14, 1925. Lead 2. Normal rhythm following the addition of digitalis to the quinidine therapy.

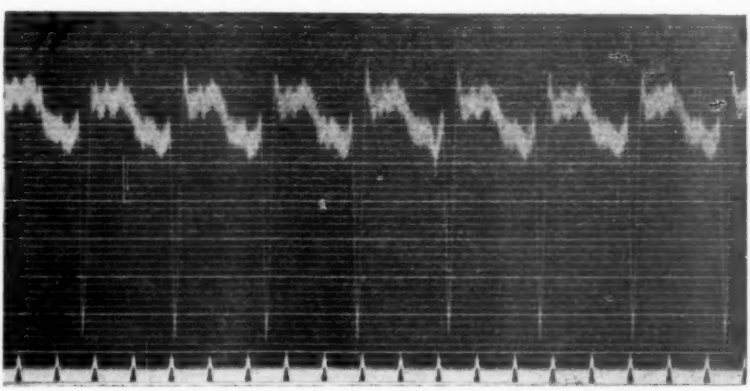

Fig. 10.—Oct. 25, 1925. Lead 2. Ventricular tachycardia. Rate 125. Note regularity of ventricular beats and probable auricular fibrillation.

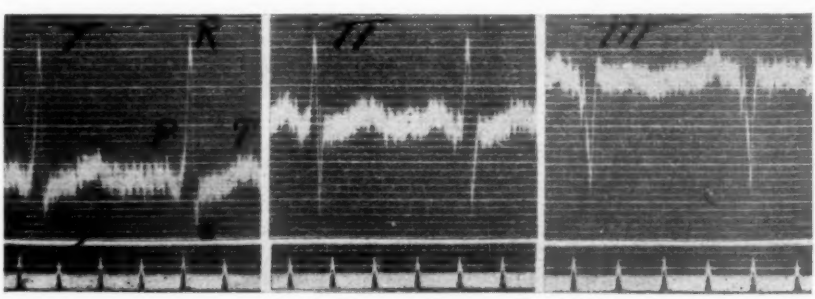

Fig. 11.—December 26, 1925. Leads 1, 2 and 3. Normal mechanism.

0.8 gm. of quinidine three times a day without digitalis. This has restored the normal mechanism (Fig. 11) and now for twelve weeks he has felt quite well and is at present at work.

CASE HISTORY

The patient, a forty-eight-year old salesman, complained chiefly of shortness of breath. There was no previous history of chorea, rheumatic fever, scarlet fever, or tonsillitis. Twenty-seven years previously, he fell to the floor after strenuous physical exertion and noticed his heart beating rapidly and irregularly. For the next nine years, he continued to do work involving considerable physical effort without unusual symptoms except when troubled with coryza or pharyngitis. At such times, he often noticed that his heart "fluttered" rapidly and irregularly and he experienced some shortness of breath. For the past few years, he has been troubled with attacks of shortness of breath coming at irregular intervals but more frequently of late. They were more prone to occur when the patient was very tired and usually appeared at night, awakening the patient out of a sound sleep. At such times, he was awakened suddenly, felt stifled, and was forced to sit up to get his breath. The attacks lasted for about an hour and gradually passed away, the patient feeling entirely well the next day. With each attack, there was severe coughing productive of slimy mucus. For the last two weeks, there has been attacks of short stabbing pains low down in the left chest which were not related to exercise or emotions.

Ten days before entering the hospital, the last attack began but did not improve as had the former ones, and after going to work he experienced a drenching sweat with rapid and irregular heart beat. The next day, the heart action still being irregular, the family physician was called. During the following few days the patient was digitalized to the point of nausea without improvement, the drug being discontinued one week before entering the hospital. During the ensuing days, there was little change in his condition, shortness of breath continuing to be quite distressing.

Physical examination showed a well-developed, somewhat overnourished man lying comfortably in bed. Respirations were only slightly elevated in rate. The heart was enlarged to percussion, the right border dulness being 5.0 cm. and the left border dulness 12.0 cm. from the midline. There was a slight thrill, apparently with systole, and the apex impulse was faint. The sounds were ticktack in quality, the first sound at the apex having a rumbling character, but there was no definite murmur. The rhythm was very irregular. The liver was enlarged. A few moist and musical râles were heard at the base of each lung. The abdomen and extremities were negative. Blood pressure was systolic 90 mm. and diastolic 80 mm. A seven foot x-ray of the heart showed the right border 5.0 cm. and the left border 10.9 cm. from the midline, while the internal diameter of the chest was 27.6 cm. The vital capacity of the lungs was 1,500 c.c. or thirty-four per cent normal. Clinical pathological tests showed nothing unusual. The electrocardiographic tracing showed auricular fibrillation and ventricular tachycardia (Fig. 1.).

Details of therapy are shown in Fig. 3. and Table I. The patient was digitalized, receiving 2.7 gm. of digitalis folia in twenty-two doses over a period of eight days. At the end of this time, the electrocardiographic tracing (Fig. 2.) showed no essential change in the condition except for a slight increase in the heart rate. There were no supraventricular beats and the ventricular tachycardia was more rapid. On the third day following the last dose of digitalis, quinidine was begun in doses of 0.2 gm. The individual dosage was increased 0.1 gm. daily so that, on the second day, the patient received 0.3 gm. three times a day and so on. During this period, the patient's clinical appearance was very bad. Respirations were only slightly elevated in rate but were labored and, at times, were Cheyne-Stokes' in character. There was slight cyanosis and the patient felt extremely weak and uncomfortable. The heart rate continued to be rapid and very irregular

and there was a marked pulse deficit (Fig. 3.). On the seventh day, shortly after the patient had received one dose of 0.8 gm. of quinidine, the pulse was found to be regular, and the electrocardiographic tracing (Fig. 5.) showed normal curves and a rate of 73 per minute. On physical examination, there could now be heard at the apex the typical late diastolic crescendo murmur of mitral stenosis. Associated with this change, there was marked symptomatic improvement and two days later the vital capacity of the lungs had increased about 42 per cent. The dosage of quinidine was immediately decreased to 0.3 gm. three times a day and the condition remained essentially unchanged for fourteen days when, after an emotional upset, the former irregular rhythm returned. Increasing the quinidine dosage was again followed by a return to regular rhythm. Similar transient attacks of irregularity (Fig. 6.) occurred on two other occasions but, in general, the patient continued to show symptomatic and clinical improvement (Fig. 7.) and was allowed to return home after fifty-one days in the hospital. Quinidine was continued in dosage of 0.6 gm. three times a day.

Since that time, he has reported at intervals of about two weeks for electrocardiographic tracings and examination. (For reference, see Table I.) Two weeks after discharge from the hospital, the electrocardiographic tracing showed impure auricular flutter but no ventricular tachycardia (Fig. 8.). This, probably, was the result of quinidine on the original auricular fibrillation. It was then thought wise to try the effect of combining digitalis with the quinidine. Two weeks later, a normal rhythm (Fig. 9.) was again present and quinidine was discontinued. On digitalis alone, however, the original disturbance recurred. It then seemed more difficult to control the condition with quinidine while he was taking digitalis so the latter was discontinued entirely. The patient was able to work as a furniture salesman for about a month, but in October began to feel very tired, had a slight cough, and was conscious that his heart was almost continuously irregular. A few days later, he experienced a sudden severe pain in his left chest which radiated up to the left shoulder and part way down the arm. Nitroglycerine gave immediate relief. Quinidine was discontinued and, five days later, he was again admitted to the hospital in order to determine the exact dosage of quinidine alone that would be necessary to maintain a constantly regular heart rhythm. After receiving two 0.6 gm. doses of quinidine, the heart became regular and remained so for eleven days when the irregularity returned, apparently, as on other occasions, influenced by the excitement of the prospect of going home. The dosage was increased to 0.8 gm. three times a day and two days later the heart became regular. On this dosage, the heart has remained regular, (Fig. 11); there seem to be no toxic effects from the continued use of large doses of quinidine, and the patient has returned to work.

SUMMARY

The clinical details of a case of mitral stenosis showing both auricular fibrillation and ventricular tachycardia are here reported. The therapeutic problem was difficult because, under full doses of digitalis, the condition remained uncontrolled and the patient grew worse. Constant administration of large doses of quinidine proved effective, inhibiting both the disturbance in the auricles and in the ventricles. As a result, a normal rhythm has been restored and the patient enabled to return to work.

ON THE DIAGNOSIS OF PERICARDIAL EFFUSION

WITH SPECIAL REFERENCE TO PHYSICAL SIGNS ON THE POSTERIOR ASPECT OF THE THORAX

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IN THIS consideration of a subject as familiar as that of the diagnosis of pericardial effusion no attempt will be made at a systematic discussion of all of its many aspects. It is my purpose to point out certain erroneous views still very commonly held and to discuss certain features not generally appreciated which, it seems to me, are worthy of emphasis. Since what is to be said relates chiefly to the larger accumulations of liquid, only effusions of the inflammatory type will be considered.

CAPACITY OF THE PERICARDIAL SAC

The experimental injection of the normal pericardial sac after death has long been a favorite form of experiment and has been done in many ways and with many different forms of injecting fluid. The results of these experiments, although far from uniform, are, however, in general agreement as to the fact that the injection of from 150 to 200 c.c. of liquid is sufficient to fill completely the complementary spaces of the pericardium and to distend the sac. The further introduction of liquid can be made only under pressure, and most experimentors are agreed that not more than from 500 to 800 c.c. can be injected into the adult pericardium even under very high pressure, and then only after the heart's walls have been collapsed and its content of blood emptied into the great vessels. (Schaposchnikoff,[1] Schüle,[2] Curschmann,[3] Williamson.[4])*

When, now, we consider that there is much unimpeachable evidence to show that, in inflammatory states, the pericardial sac very frequently contains from 1500 to 2000 c.c. of serous exudate, and that occasionally much larger amounts have been shown to occur (up to 4000 c.c.), it becomes evident that the information derived from the rapid injection of the normal, unyielding pericardium cannot safely be applied to the wholly different conditions which obtain when an inflamed, succulent, yielding membrane is gradually, over a period of days or weeks, distended with inflammatory exudate. For our purposes, then, in considering the capacity of the inflamed pericardial sac, it is well to forget

*In the recent careful experiments of Williamson, 655 c.c. was the largest amount of liquid he was able to inject without either rupturing the sac or stripping it off from its attachment to the great vessels.

the experimental facts and to concentrate attention upon the purely clinical evidence which is so abundant and so illuminating.

PERSISTENCE OF THE PERICARDIAL FRICTION MURMUR DURING EFFUSION

One of the views firmly fixed in the minds of most physicians is that, with the accumulation of any considerable amount of serous exudate, the two layers of the pericardium at once become separated and the friction murmur disappears. The logical corollary to this assumption is that if the friction murmur be plainly audible over any considerable portion of the precordium one may safely conclude that there is little if any liquid present. Although warnings that this conclusion is quite unjustified have not been lacking and are to be found scattered through the foreign literature as well as through our own (Schaposchnikoff,[1] Curschmann[3], Blechmann[5], West[6], Thayer[7], Williamson[4]), nevertheless the idea that the friction sound may be expected to disappear whenever liquid begins to accumulate in the pericardial sac is still one of the cherished traditions of the diagnosis of pericardial effusion. How incorrect this view is may be seen from the fact that among thirty-four cases of pericarditis with frank signs of effusion observed during the past five years in the First Medical Division of the New York Hospital and in private practice, a pericardial friction sound was noted in twenty-four cases (70 per cent) during the time that the presence of an effusion could be clearly demonstrated. In many of these cases the friction sound could be heard over a large part of the precordium throughout almost the whole period during which the effusion was present. The reason for this apparent paradox will be considered later.

BEHAVIOR OF THE CARDIAC IMPULSE AND APEX BEAT

What has been said concerning the persistence of the friction murmur during the stage of effusion applies also, to some extent, to the cardiac impulse and the apex beat. In a considerable proportion of the cases a diffuse, wavy, cardiac impulse may be seen and felt over the body of the heart, and not infrequently a distinct apex beat may be recognized, even in the recumbent position, at a time when the pericardium can be shown to contain a large quantity of liquid. These statements run counter to the view generally held but are none the less true.

The prevalent opinion that, when the pericardium is distended with serous exudate, the heart recedes from the chest wall and is separated from the latter by a thick stratum of liquid is the outcome of the teaching of Skoda and most of the later standard German writers who believed that the heart, because of its greater specific gravity, sank to the depths of the distended pericardial sac. Although this view has been shown to be incorrect by Schaposchnikoff, by Curschmann and

by various French and English clinicians, it still remains the generally accepted one; chiefly, apparently, because it seems on first thought the natural and reasonable thing to expect. In a majority of the cases with effusion the apex beat disappears and the heart sounds at the apex become faint, but it has often been shown that even in these cases the heart, except perhaps at its apical portion, nevertheless lies close to the anterior chest wall and indeed can occupy no other position. This conception of the heart as sinking deep into the chest and as being separated from the anterior chest wall by a thick layer of liquid is responsible for the choice of points close to the sternum (either to the left or to the right and either within or just without the line of the internal mammary artery) as the conventional sites for puncture of the pericardium. Anyone who has had much experience with tapping the pericardium at these sites must have convinced himself that while it is very easy to obtain heart's blood it is usually very difficult to secure more than a few drops of pericardial liquid.

A brief review of some of the anatomical relations will suffice to show why the heart must remain in contact with or close to the chest wall under all conditions. In Fig. 1, which represents a transverse section of the chest at the level of the fourth costal cartilage and the body of the seventh dorsal vertebra, it will be seen that the heart fills completely the space between the anterior chest wall and the vertebral column. The accumulation of any considerable quantity of liquid in front of the heart would be possible only by the complete dislocation of the heart into the left half of the thoracic cavity. In Fig. 2, the broken line represents the heart's axis of fixation, which runs somewhat obliquely from above downward and to the right, the chief points of fixation being the aorta and superior vena cava above, and, below, the inferior vena cava where it passes through the diaphragm. These attachments are such that the basal portion of the heart is held firmly fixed between the sternum and the vertebral column, while the apical portion is allowed considerable freedom of motion. Although it is possible that this latter part of the heart may in some cases be displaced somewhat dorsally by the accumulating liquid in the pericardium it seems certain that in most cases this apical portion also lies close to the chest wall, even when the apex beat cannot be recognized. Schaposchnikoff[1] believes that the elastic pull of the great vessels is chiefly responsible for the maintenance of the apical portion of the heart in contact with the chest wall.

The certainty that the heart must remain in close apposition with the chest wall is made greater by the fact that, in a large proportion of the cases at least, the heart is enlarged. In the rheumatic form of pericarditis, which in my own series accounted for 75 per cent of all the cases, it is the rule to find some preexisting valvular damage and some enlargement of the heart. Moreover, there is reason to believe

that in every case of pericarditis the inflammation of the visceral layer is accompanied by inflammation of the underlying myocardium, which in turn results in loss of the normal tone and in general dilatation of the organ. This point has been emphasized by West.[6]

If it is necessary to abandon the concept that in pericarditis the

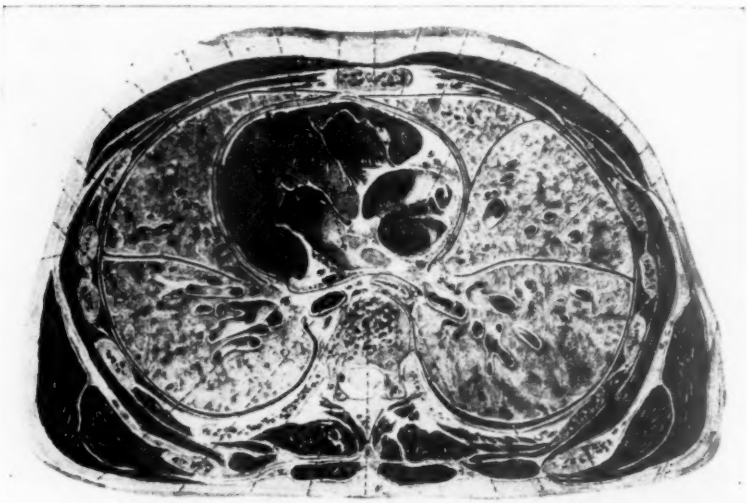

Fig. 1.—A transverse section of the normal thorax, at the level of the fourth costal cartilage and seventh dorsal vertebra, showing the heart filling completely the space between the anterior chest wall and the vertebral column. (From Spalteholz's Hand-atlas.)

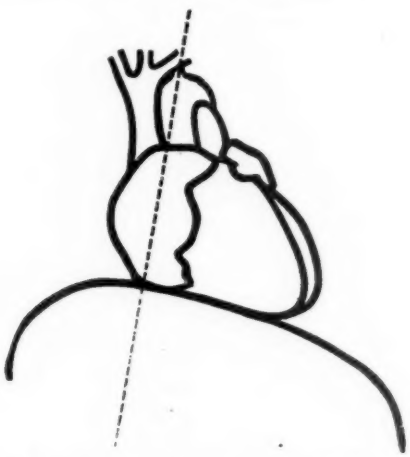

Fig. 2.—The broken line indicates the axis of fixation of the heart by its attachments. (From Curschmann.)

heart sinks to the depths of the distended sac, it is no less necessary to discard the view, so vigorously advocated by Potain and concurred in by various other authors, that in large effusions the apex of the heart is displaced upward and to the left so that its beat can often

be located in the third intercostal space. It is true that an impulse can frequently be felt in this position, but this impulse is not that of the apex beat. It is an impulse of the left side of the body of the heart, felt more distinctly than usual because of the retraction of the border of the left lung (Ewart). The fact seems to be that in pericardial effusion the position of the heart undergoes no material change but remains approximately normal.

PERCUSSION OUTLINES

The varying contours of the percussion outlines on the front of the chest have been so often discussed and are so well understood that little need be said upon this point. These contours show many variations which are dependent upon several factors: the habitual posture of the patient (whether recumbent or more or less erect), the anteroposterior diameter of the thorax, the presence or absence of adhesions of the lung borders, etc. The most significant early changes from the normal outline of cardiac dulness are the appearance of marked dulness behind the manubrium and in the first and second right and left intercostal spaces; the extension of the absolute dulness of the heart into the right, fifth intercostal space (Rotch's sign), and especially the extension of this dulness to the left of and below the position of the apex beat. This lower border of dulness in the apical region can usually be readily determined because of its contrast with the tympany of Traube's space.

With increase in the quantity of liquid the area of flatness assumes a roughly triangular form, with its blunt apex upward. This triangle is sometimes approximately equilateral, extending almost as far to the right of the sternum as to the left, but usually it is more nearly a right-angled triangle, with the right border almost parallel to the right border of the sternum and a few centimeters to the right of it. When the effusion becomes very large the area of cardiac dulness tends to assume a more rectangular outline in that the left border of the triangle becomes more nearly horizontal as it extends out into the axilla.

The demonstration of a progressive increase in the area of flatness and the evidence of flatness extending well below and well to the left of the apex beat are of special diagnostic significance. Morris and Little[8] have emphasized the importance of the alteration in the contour of the area of dulness upon change in the posture of the patient. In changing from the recumbent to the erect position there is a lessening of the width of the dull area over the upper part and an increase in its width just above the diaphragm.

POSTERIOR SIGNS

Ever since the time of Bamberger and of Oppolzer it has been recognized that large pericardial effusions may occasionally give signs

over the left back which simulate closely those of pleural effusion; but such posterior signs seem to have been regarded as exceptional. At any rate they have never gained general recognition as being among the usual signs of large effusions. In 1889 Pins[9] of Vienna, under the caption, "A New Symptom of Pericarditis," described the occurrence, chiefly in children, of an area of flatness or dull tympany extending from just below the angle of the left scapula to the base, with clear, bronchial breathing and bronchophony and with persistence of the tactile fremitus. The essential part of this new sign, however, was the fact that, if the patient be put in the knee-elbow position, these posterior signs disappear wholly or in part, only to reappear when the patient resumes the erect position. This sign, he noted, was not to be found when the amount of exudate was small, nor was the disappearance of the posterior signs likely to occur on change of position when the quantity of exudate was very large. Although the accuracy of Pins' observation has been confirmed by various writers, chiefly among the French, his quite important contribution has thus far failed to receive general recognition.

Ewart,[10] writing in 1896, included among his twelve "diagnostic signs" of pericardial effusion one which he terms "the posterior pericardial patch of dulness," a small rectangular area of relative dulness at the left base (ninth to twelfth rib), usually extending slightly to the right of the vertebral column. He also speaks of a small area of tubular breathing and egophony heard just below the angle of the left scapula. All through the literature of pericarditis, indeed, may be found scattered references to these pseudopleuritic signs over the left chest posteriorly. Christian,[11] in an interesting paper read before the American Medical Association in 1918, entitled "The Frequency of Pulmonary Compression Signs in Acute Fibrinous Pericarditis," gives his experience with fifty-three cases of acute pericarditis seen in the Brigham Hospital, in 73 per cent of which there were signs over the left lower back. These cases, he says, "were not patients with signs indicating extensive pericardial effusion." They ordinarily "would be diagnosed as acute or fibrinous pericarditis because of a friction murmur over the precordium." In a few cases the attempt was made to tap the pericardium, but no fluid was obtained. In one cited case the left back was tapped and 300 c.c. of liquid withdrawn, which was assumed to be pleural fluid. In another case, with autopsy, there was a "slight excess" of fluid in the pericardium and some also in the left pleural cavity. He concludes that these posterior signs are in part due to pleural effusion but that they probably cannot be ascribed to an associated pneumonia.

Christian, then, emphasizes the frequency of posterior signs in pericarditis but believes that these signs are frequently to be found in cases in which there is little or no effusion. The significance of his

conclusions turns very largely upon the question of diagnosis; upon what constitutes evidence for or against the presence of liquid. Can liquid be excluded merely upon the presence of a friction murmur or even by the failure to find liquid by tapping the pericardium at the points usually recommended for tapping? I am convinced that it cannot. Indeed, I am convinced that the very existence of these posterior signs constitutes in itself evidence of the presence of pericardial fluid. This evidence is not always conclusive, for occasionally pericarditis is complicated by a left pleural effusion, but such cases are after all not so very common, and the absence of pleural fluid can usually be shown by the appearance of x-ray plate.

PERSONAL EXPERIENCES

For a good many years I have been interested in and puzzled by these posterior signs. I have found them not only on the left side but on the *right* as well in cases of pericarditis which, it was assumed could not, because of the presence of a friction sound, be associated with much effusion. In a number of the cases, suspecting liquid because of the posterior signs, the pericardium was tapped at one or other of the conventional sites without success. Not until I became familiar (several years after it was published) with Curshmann's classic article[3] on pericardial effusion and studied his instructive illustrations did I gain a satisfactory understanding of the behavior of the pericardium in the presence of a large inflammatory exudate and realize that these posterior pseudopleuritic signs were the natural and logical outcome of the pathological conditions present.

Such posterior signs vary greatly. There may be merely a small area of impaired resonance at the left base close to the spine, with some diminution of the vesicular murmur and a slight change in the voice sounds. On the other hand there is often an extensive area of flatness over *both* lower chests, with absence of the vesicular murmur and with clear bronchial breathing and bronchophony (or egophony) over the upper and outer border of this area of flatness. Usually the tactile fremitus is not entirely lost even over the flat area. Adventitious sounds are commonly lacking, but there may be fine râles along the upper margin of the dull area. Occasionally the bronchial breathing may be so intense as to simulate that heard over hepatized lung, but usually it has the faint, distant character commonly found in pleural effusion. In my own experience the dull area, even when small, has never had the rectangular outlines described by Ewart. While in most cases the signs described are more distinct and extensive over the left side of the back there are occasional instances in which they are more pronounced on the right side. Among the thirty-four cases studied there were six in which no abnormal posterior signs were noted; in seven cases the signs were confined to a limited area of

dulness at the left base, with a small area of bronchial breathing near the lower angle of the scapula; in one case this patch of bronchial breathing was present in both sides, with little or no dulness; in one case there was moderate dulness on the left side, slight dulness on the right side, but no bronchial breathing; in fifteen cases there were frank signs of fluid on both sides, the signs being more extensive on the left, whereas in the remaining four cases these signs were more pronounced upon the right side.

In a few cases in which it has been possible to watch the development of the posterior signs as the pericardial liquid accumulated, the first change has usually been the appearance of a small area of bronchial breathing just above and within the lower angle of the scapula. This change in breathing has been noted even before any distinct dulness could be detected. The explanation for this patch of bronchial breathing in effusions too small to give frank signs of fluid over the posterior aspect of the thorax is by no means clear. It cannot be due to pulmonary compression, for the area of pulmonary resonance shows that there has been little retraction of the lung and certainly no compression. It seems possible to me that it may be due to the fact that the upper part of the distended pericardial sac, lying as it does upon the left main bronchus, may compress this against the body of the sixth dorsal vertebra, so that the vertebra and its attached rib may convey bronchial sounds to the back which ordinarily are not audible there.

When the effusion is large and the posterior signs typical the area of flatness on each side of the spine assumes roughly the shape of a right-angled triangle, with the apex in the interscapular region, well above the scapular angle, the base corresponding to the base of the thorax, and the oblique side extending downward and outward about to the posterior axillary line; the flatness there shading off gradually into pulmonary resonance. In most cases the triangle of flatness is distinctly smaller on the right side than on the left, but it is rarely lacking entirely when there is even a moderately large area of flatness on the left side. This right-sided flatness or dulness has been present in cases in which the radiographic films have indicated only a small amount of liquid in the right pouch of the pericardium. In such cases is seems probable that the right-sided dulness is to be explained by the damping effect upon the normal sound vibrations of the distended pericardial sac lying upon and hugging the bodies of the lower dorsal vertebrae; in other words, that the dulness is produced in much the same way as it is supposed to be produced in Grocco's triangle of dulness on the right side in left-sided pleural effusions.

The reason for these striking posterior signs in the case of large pericardial effusions will be understood if one considers that, since the increasing volume of exudate can find no space either directly in front of or behind the heart, it must occupy chiefly the lateral portions of the

pericardial sac. As the liquid increases day by day and the inflamed and succulent membrane yields steadily before the increasing pressure, the weight of the liquid will cause a sagging of the sac which, with the patient occupying the recumbent or semi-recumbent posture, will be backward along each side of the vertebral column. In the upper part of the pericardium this backward pouching of the sac is interfered with by the fact that it lies upon the two main bronchi, but below the roots of the lungs (sixth dorsal vertebra), each lateral pouch of the pericardium is free to extend dorsally along the side of the bodies of the vertebrae until it reaches the posterior thoracic wall. A glance at Figs. 3, 4, and 5, which are reproductions of Curschmann's semi-

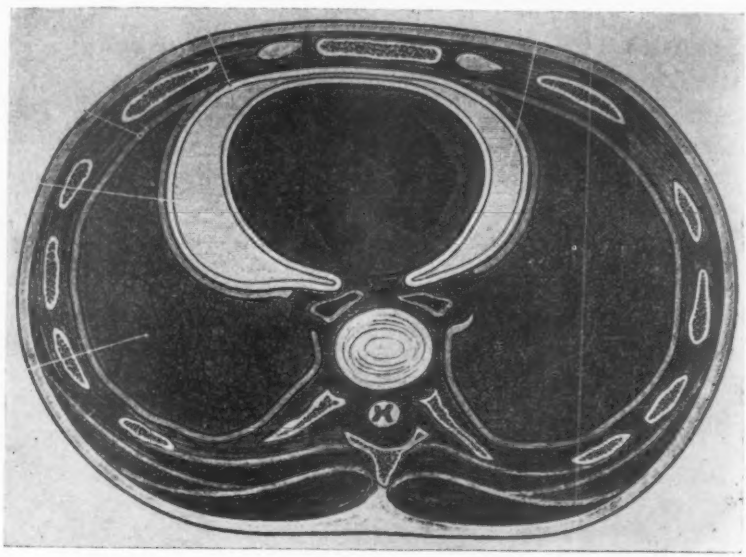

Fig. 3.—Semidiagrammatic view of a transverse section of the thorax showing the disposition of the liquid in a small pericardial effusion. (From Curschmann.)

diagrammatic illustrations, will serve to make the situation clear. Instead, then, of picturing the distended pericardium as of more or less globular shape, with the heart surrounded on all sides by liquid, it is more nearly accurate to think of it as a double pouch hanging over the heart and vertebral column, much as a pair of overfilled saddlebags would hang over the saddle and sides of a horse.

In order to make such a conception of the distribution of pericardial effusion at all convincing it is necessary to keep in mind the two essential facts: first, that the inflamed pericardial sac, in contrast to the normal one, is capable of almost indefinite enlargement when the distention takes place gradually, and, second, that the quantity of liquid found in pericardial effusion is usually surprisingly large. It is by no means unusual to find the sac containing from 1500 to 2000 c.c. of

serous exudate and, as has been said, there are many authentic records of cases showing much larger amounts.

Retraction of the corresponding lung keeps pace with the increase in

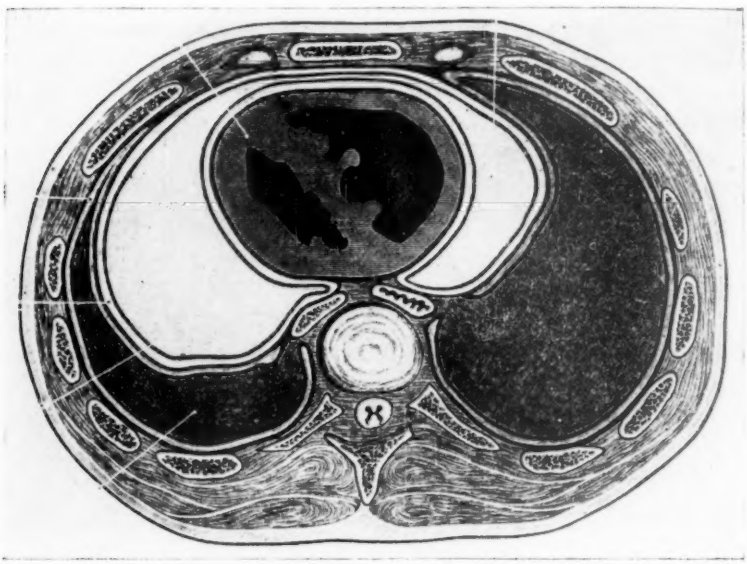

Fig. 4.—Transverse section of the thorax (semidiagrammatic) showing the location of the liquid in pericarditis with moderate effusion. (From Curschmann.)

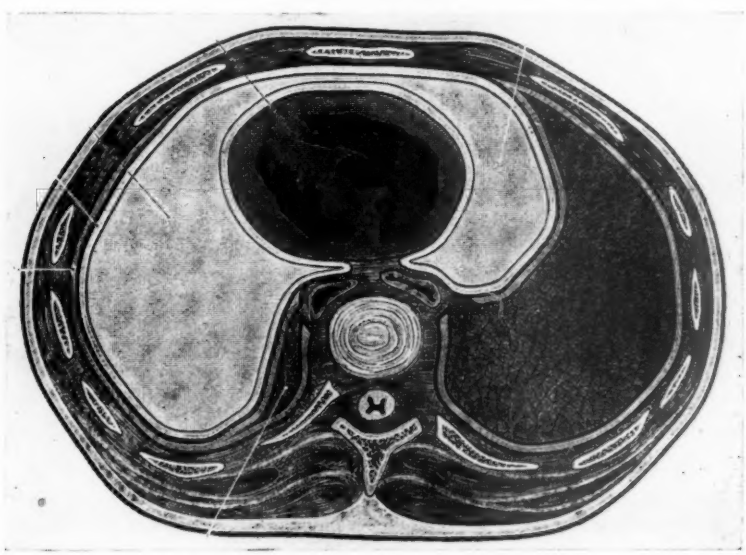

Fig. 5.—Shows the disposition of the liquid in a large pericardial effusion. Note the compressed left lung indicated as lying against the vertebral column. (From Curschmann.)

the size of each lateral pouch, and eventually, if the effusion be large, the shrunken lower lobe is compressed into a small compass. The posi-

tion of this compressed remnant of the lower lobe is of some interest. In Curschmann's illustration (Fig. 5) the left lung is represented as being compressed against the vertebral column and the pericardial sac as being in contact with the ribs throughout the entire circumference of that half of the thorax. My own experience leads me to think that the compressed lung lies, not against the vertebral column, but against the ribs in a region corresponding to the posterior part of the axilla, for at this point I have always found some pulmonary resonance, even in the case of very large effusion. Moreover, as the pericardial pouch enlarges and begins, below the root of the lung, to extend backward along the side of the bodies of the vertebrae, it must, it would seem,

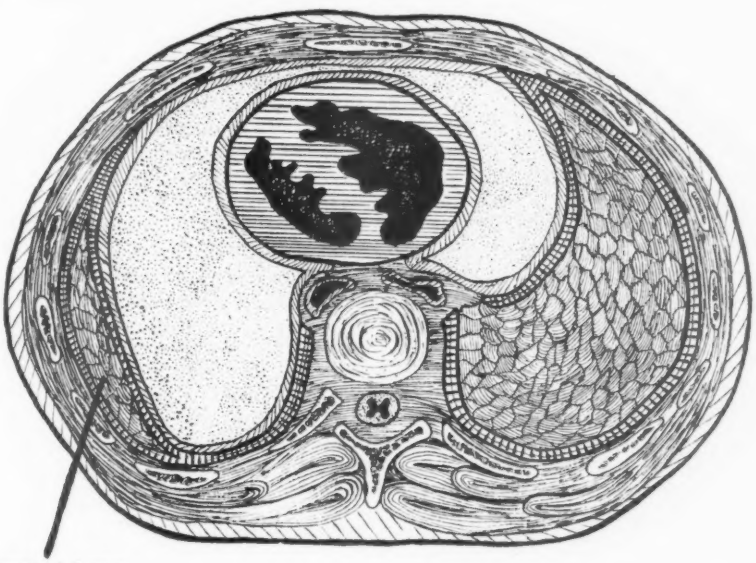

Fig. 6.—Illustrates the author's view as to the usual position of the compressed left lung in the presence of a large pericardial effusion.

work its way between the vertebrae and the inner surface of the lung. It is difficult, indeed, to see how the compressed lung can ever lie against the vertebrae. Fig. 6 indicates what seems to me to be the usual position of the compressed lower lobe.

SITES FOR TAPPING

Although foreign to the subject of this article, it seems desirable in closing to say a few words concerning the proper sites for aspiration of the pericardial sac, when that is deemed necessary. The locations usually recommended are those close to and to one or the other side of the sternum. These points were chosen in order to avoid the necessity of passing through the pleura to reach the pericardium and in the belief that the heart lay sufficiently deep in the chest to escape danger

of puncture. The fact is, however, that the heart lies in close contact with the chest wall and can hardly escape injury if the tap be made at any of these points. It is obvious that, in order to reach any considerable amount of liquid, the needle must enter one or the other of the two lateral pouches, and where the distended pericardial sac is pressed firmly against the chest wall the objections to passing through the pleura seem to be wholly theoretical, except in the case of purulent effusions. In the case of rheumatic effusions there is, of course, no such danger, and the needle should be inserted either at a point well to the left of and below the position of the apex beat or over the area of flatness posteriorly. At either of these sites one is reasonably certain of being able to withdraw sufficient liquid to justify the procedure. In recent years I have come to prefer the posterior tap as being the simplest and the safest. It should be added, however, that, in my judgment, most rheumatic effusions do not require aspiration. The question of aspiration in the case of effusions which are probably purulent is much less simple. When the pericarditis complicates lobar pneumonia, or any of the pyemic or septic diseases, the effusion is almost certainly seropurulent or purulent, and puncture through pleura should be avoided. If an exploratory puncture be deemed necessary before operation, the safest point for aspiration is probably the space between the ensiform process and the left costal margin. In that case the needle should be directed slightly upward and sharply backward and to the left in order to avoid the heart and to reach the left lateral pouch of liquid.

SUMMARY

In the preceding pages I have attempted to show that: (1) The results of the experimental injection of the normal pericardium after death, with respect to the distribution of the liquid in the sac and to the amount the distended sac will contain, cannot safely be applied to the clinical condition of pericarditis with effusion. In the latter state the quantity of liquid is often vastly greater and the shape of the distended sac entirely different. (2) A pericardial friction sound not only may be, but usually is, present when the pericardium contains a large quantity of exudate. (3) A visible and palpable cardiac impulse and apex beat also are quite compatible with the presence of a large effusion. (4) In large effusions signs suggestive of those of pleurisy with effusion are regularly found, not only over the left back, but over the right back as well. (5) On the right side these signs are sometimes present when the appearance of the x-ray films indicates that the right pouch of the pericardium contains only a relatively small quantity of liquid. (6) In such cases the signs probably are produced as they are supposed to be in Grocco's triangle of dulness in pleural effusion.

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ADHERENT PERICARDIUM WITH CALCIFICATION

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ADHERENT pericardium may be suspected when, with a history suggestive of pericarditis, the patient has manifested symptoms of cardiac incompetency not associated with, nor believed to be due to disease of the valves, disease of the aorta, or vascular disease with hypertension. Symptoms of cardiac incompetency in such patients are often ascribed to myocarditis,—an indefinite term which frequently fails to take into account causes for the disturbance outside the heart muscle itself, such as an earlier infective process which has involved the mediastinum and pericardium.

The pericardium lies in intimate contact with the structures of the mediastium. Involvement of these structures occurs not infrequently during the course of infections such as pneumonia with empyema, rheumatic fever, scarlet fever, pyemia, and tuberculous pleurisy with effusion. The subsequent pathological changes leading to fibrous tissue adhesions between the visceral and parietal layers of the pericardium may produce little disturbance of heart function, even when more or less obliteration of the pericardial cavity has occurred, provided the heart's contractile efforts are unimpeded by extrapericardial adhesions to the chest wall, to the diaphragm, to the pleura, or to the mediastinal structures. The extrapericardial adhesions to bony inelastic structures, such as ribs or sternum, are particularly serious impediments to the contractile power of the heart and soon lead to symptoms of cardiac insufficiency. W. H. Smith[1] in a study of 3053 necropsies found 62 instances, or 2 per cent, of adhesive pericarditis. The condition occurred about twice as often in males as in females.

The signs and symptoms of importance in the diagnosis of adherent pericardium are:

1. The history of an earlier empyema, rheumatic fever, scarlet fever, pyemia or tuberculous pleurisy with the subsequent development of symptoms of cardiac incompetency extending, as a rule, over a period of years.

2. The development of symptoms, such as dyspnea, cyanosis or anemia, which appear to be out of proportion to the apparent signs of heart disease; that is, the valve tones may be quite clear, the rate and rhythm not markedly disturbed, and the size of the heart not greatly increased.

3. Fixation or retraction of the apex beat may occur, but frequently its accurate location is difficult. McPhedran[2] has regarded a systolic rhythmical retraction in the lower part of the precordial area, when present, as the most important sign of adherent pericardium. When confined to the region of the the apex beat, the sign may not be of material value, but when associated with retraction of the costal

cartilages near the sternum, it possesses diagnostic significance. With chronic adhesive pericarditis of long standing the heart may be greatly enlarged and produce asymmetry of the chest wall.

4. Under normal conditions of inspiratory effort, more expansion occurs in the anteroposterior diameter of the chest than in the lateral diameter. Keith[3] and Wenckebach[4] have noted that with adhesions between the pericardium and the chest wall an increase in lateral expansion occurred.

5. Under normal conditions the chest is lifted upwards during inspiration, while

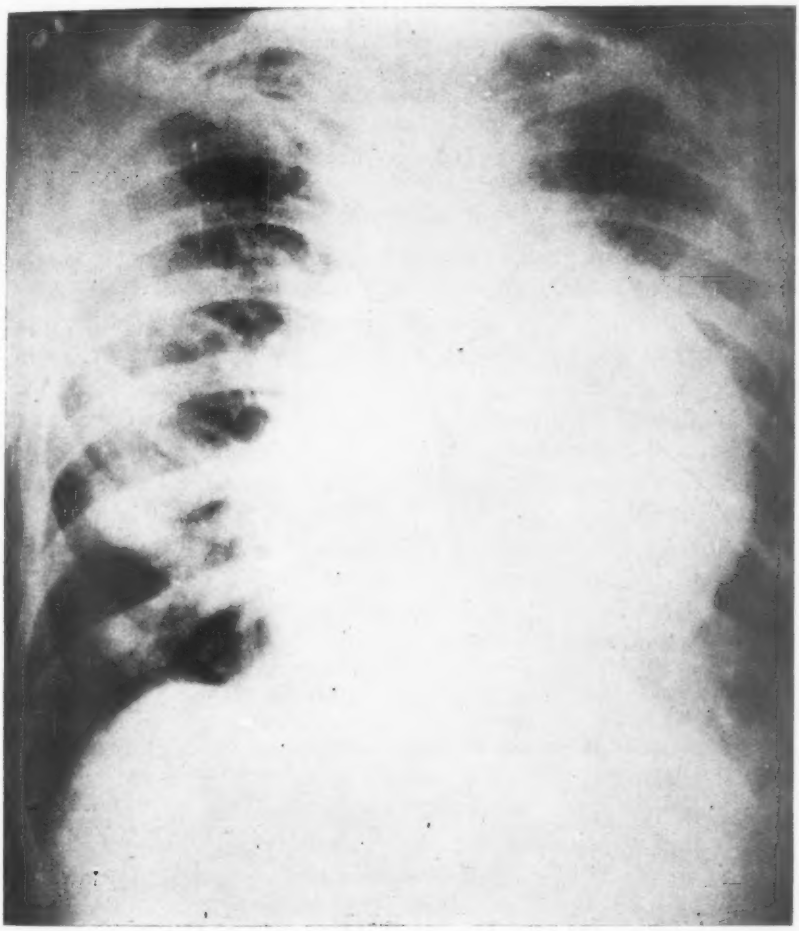


Fig. 1.—Purulent pericarditis and adhesive mediastinitis with rotation of heart toward the back. Five aspirations of pericardium with recovery.

synchronously the epigastrium protrudes forward. When adhesive pericarditis and mediastinitis have occurred, the lifting movements of the upper chest above the apex, may be greatly restricted, while the epigastrium may recede during inspiration. Such fixation or limitation of movement of the upper chest constitutes an important objective symptom. Its importance was first emphasized by Sibson[5] in 1877.

6. With retraction of the lung due to pleural adhesions, deviation of the trachea toward the affected side usually occurs. In pleuro-pericardial adhesions with re-

traction of the lung and cardiac displacement, such deviation toward the left may be present. The trachea can best be palpated above the clavicular-sternal junction in the jugular fossa. Webb and his associates[6] have described the deviation present in tuberculous retraction of the lung associated with pleural adhesions.

7. I have noted[7] at various times in patients with mediastinitis and pericarditis complicating pneumonia, a definite friction rub synchronous with the heart action, below the angle of the left scapula when the rub could not be detected over the anterior chest. The explanation of its occurrence probably depends upon a backward displacement of the heart as a result of mediastinal adhesions. The transmission of this posterior friction rub is clearer if the lower lobe of the left lung is consolidated or compressed, while the rub may be less audible or absent when free fluid is present in the left pleural cavity. The rotation of the heart above described is illustrated in Fig. 1, reproduced from the roentgenogram of a patient with pericarditis and mediastinitis.

8. By fluoroscopy diminished systolic and diastolic excursions of the edge of the cardiac shadow may occur. The heart may appear to be fixed, with immobility of the diaphragm, when the patient is in the lateral position.

As a rule more dependence must be placed upon associated signs for the diagnosis of adhesive pericarditis since the symptoms are frequently masked or latent. With adhesive pericarditis of sufficient extent to produce symptoms, polyserositis is usually associated and fluid can be demonstrated in the pleural cavities or in the peritoneal cavity. The condition differs from that seen in stasis from heart failure, in that until the later stages of the disease, the limbs are not swollen. The liver enlarges comparatively early in the course of the disease and is larger than that seen in chronic passive congestion. Little or no jaundice occurs. A diagnosis of liver cirrhosis has frequently been made in such cases. In 1896 Pick[8] described the condition as "pericarditic pseudocirrhosis of the liver." In two of his cases obliterative pericarditis with calcification had occurred.

CALCIFICATION OF THE PERICARDIUM

The deposition of lime salts in connective tissue which has been produced as a result of a chronic inflammatory process is not an unusual pathological finding. In the heart such deposition may occur in the endocardium, especially about the subendocardial tissue of the valve flaps and rings. It may also be noted in the myocardium. Such deposits are rare, but occurred in Cutler's and Sosman's two cases. As a rule, the pericardium is more extensively involved than the myocardium. Youmans and Merrill[18] have reviewed 104 reported cases, 94 of which were discovered at autopsy.

Since the interpretation of signs and symptoms may be inconclusive the main reliance in making a diagnosis of this condition will depend upon roentgenoscopy. The examination should include stereoscopic films in both the anteroposterior and oblique positions. Under the fluoroscope, areas of increased density in the heart shadow, calcified plaques in the pleura or upon the dome of the diaphragm, may be evi-

dent. Fixation of the apex, and failure of the apex to descend upon inspiration, as well as obliteration of the normal diaphragmatic contour are important variations from the normal when adhesions are present.

Schwartz[9] in 1910 reported the first instance of calcified pericardium diagnosed, during life, by means of roentgenoscopy. In 1911 he added one more to the literature. Since then additional instances have been reported by Groedel,[10] Rieder[11] (two cases), Weil,[12] Klason,[13] Brauer,[20] Assman,[14] Case,[15] Amundsen,[16] Scholz,[17] Youman and Merrill,[18] and by Cutler and Sosman[19] (two cases).

To this list of fifteen cases diagnosed by roentgenoscopy one more may be added.

E. M. S., male, aged fifty years, was seen Feb. 15, 1923. His chief complaint was shortness of breath on exertion, an enlarged liver and swelling of the legs. The illness responsible for his condition developed at the age of eighteen years. It consisted of a left sided pleurisy with effusion and ascites, which lasted for about three months. At this time aspiration of the chest was performed and two gallons of fluid were obtained, after which by means of diuretics, the ascites disappeared. He was then in fairly good health for seventeen years when, at the age of thirty-five, edema of the legs and swelling of the abdomen recurred, which disappeared after administration of digitalis. Eleven years later at the age of forty-six, swelling of the limbs and abdomen again recurred. The condition was then diagnosed by his physician as "liver disease."

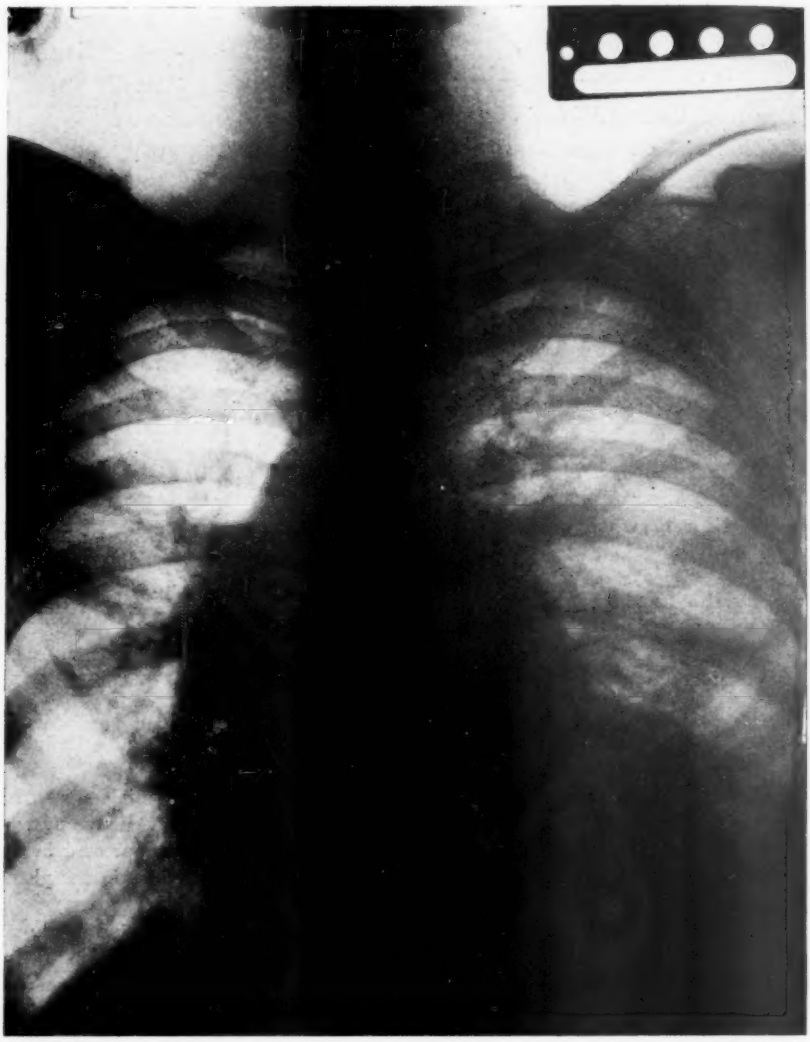
At the time of examination he had again been incapacitated for about six months by dyspnea, ascites and edema of the limbs. No history of rheumatic fever, chorea, tuberculosis, pyemia, scarlet fever or pneumonia was obtained. The physical examination revealed the heart apparently of normal size and position, except that the apex beat could be indistinctly felt, and appeared to be fixed irrespective of change in position. The rhythm was irregular, of the trigeminous type with no pulse deficit. The rate was not increased. The apex thrust, when the trunk was bent forward was diminished. Upon auscultation a presystolic rumble with a soft presystolic murmur was heard. The pulmonic second sound was snapping in character and accentuated. Upon inspiration the chest expanded more in the lateral than in the anteroposterior diameter. A pulsus paradoxus was not constantly present. The radials were small and sclerotic. The blood pressure were 100/80 mm. in both arms. Dullness over the posterior right chest extending to the angle of the scapula, with suppressed breathing and diminished vocal and tactile fremitus, was suggestive of fluid in the pleural cavity.

The liver was much enlarged and protruded beyond the costal border in the epigastrium and right hypogastrium. The surface was nodular and gave the feel of a globular mass the size of an orange in the midliver region. A moderate amount of fluid was present in the abdomen and the legs were edematous to the thighs.

The red cell count was 6,208,000 per c.mm., the white cell count 11,300 per c.mm., polynuclear cells 81 per cent, large lymphocytes 8 per cent, small lymphocytes 8 per cent, eosinophiles 1 per cent, Hg. 85 per cent (Dare). The quantity of urine in twenty hours was 1,000 c.c. and was normal to qualitative and microscopic examination. Nocturia was absent. The fasting blood chemistry showed N. P. N. 42.1 mg., preformed creatinin 1.1 mg., uric acid 3.7 mg. and sugar 90.9 mg. per 100 c.c. Wassermann examination of blood was negative. Fluoroscopic examination of the chest revealed a generalized opacity of moderate degree throughout the right lung field

suggestive of thickened pleura. No definite fluid level could be seen. The right diaphragm was higher than normal extending to the level of the fourth rib, and its surface was flattened. The right costophrenic angle was obliterated. The cardiac apex did not descend well upon inspiration and appeared to be fixed.

Films of the chest (Fig. 2), taken of the cardiac region showed a diffuse haze over the right lung field with a high and flattened right diaphragm. The left chest

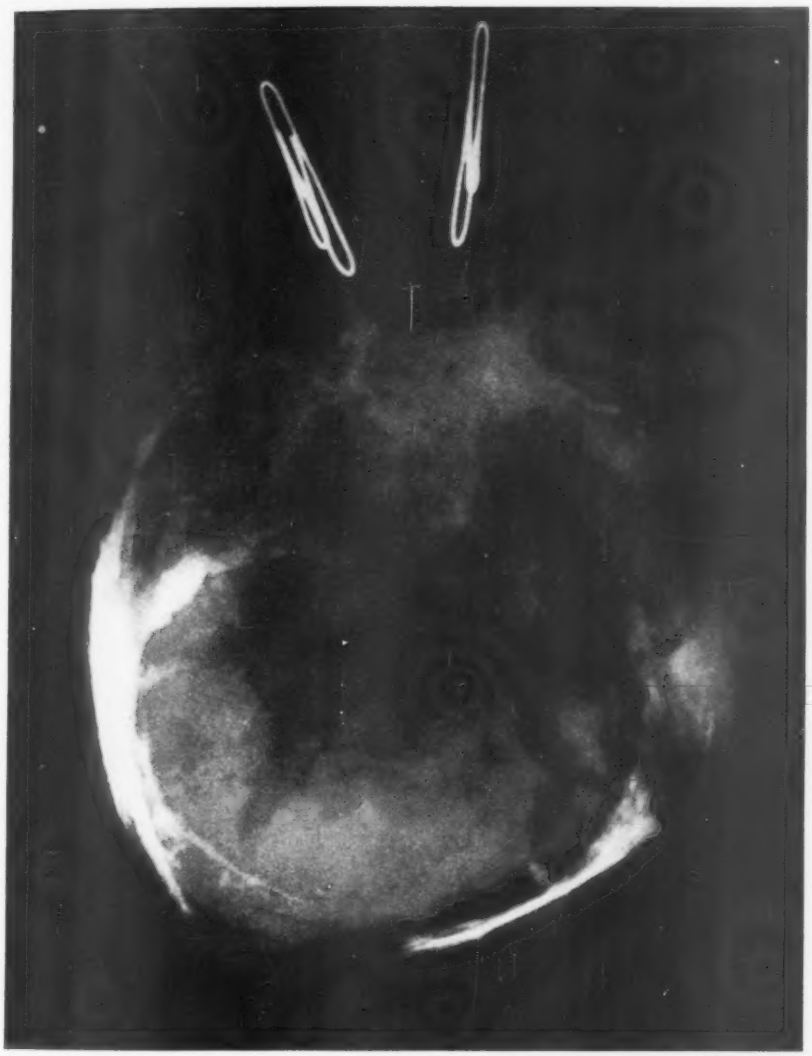


Left Right

Fig. 2.—A dense longitudinal shadow along the border of the left ventricle could be seen by fluoroscopy.

appeared clear. The heart appeared enlarged to the right and left with a swelling in the left auricular area. There was an inverted "Y" shaped white line along the left border of the left ventricle suggestive of calcification. The aorta and trachea appeared normal. On July 28, 1923, anteroposterior and oblique films of the cardiac area showed the calcification mentioned above and also some irregular areas of calcification anteriorly at approximately the region of the auriculoventricular

junction. A few scattered masses of calcification were evident just above the middle portion of the left diaphragm. There was evidence of a right-sided interlobar pleurisy. On Oct. 16, 1923, a film of the chest showed dense clouding of the right lung field with evidence of retraction of the lung suggestive of fluid. The cardiac shadow showed a white line extending from the region of the apex to the left diaphragm suggestive of a partially calcified cardiophrenic adhesion.



Left Right

Fig. 3.—Postmortem roentgenogram of heart showing extensive calcification of pericardium.

Subsequent Course.—Between February and May, 1923, the patient was able to do a moderate amount of work and was comfortable upon a diet which restricted his fluid intake. The medication consisted of digitalis in small doses alternating with theobromin sodium-salicylate and theocin. In May, 1923, 3,000 c.c. of clear sterile fluid containing a few lymphocytes was aspirated from the right chest. The

aspiration was repeated upon two occasions in July, 1923. The operation of precordial costectomy was urged at this time but the patient would not consent because of his reasonably comfortable condition. Professor Wenckebach of Vienna, who was a visitor in Pasadena in July, 1923, kindly saw the patient with me. In addition to the signs before mentioned he pointed out that the patient's upper chest was only slightly lifted upward during inspiration and that the epigastrium instead of moving forward actually receded during inspiration. (Sibson's sign.)

The Clinical Diagnosis was adhesive pericarditis with calcification, chronic pleuritis and peritonitis (polyserositis) and Pick's pseudocirrhosis of the liver.

In February, 1925, he developed bronchopneumonia with death after one week's illness. At the time of death the chronic adhesive pericarditis had undoubtedly existed between fifteen and twenty years.

Necropsy.—Upon opening the chest such extensive adhesions were encountered between the lungs and pericardium that it was almost impossible to separate them. The anterior mediastinal space was obliterated. The parietal pleurae were much thickened. Fibrous adhesions between parietal and visceral pleurae were present at both apices. The lungs were edematous and showed extensive bilateral bronchopneumonia with small atalectatic areas and pus exuding from the cut ends of the bronchioles. Section of the adherent apical portions of both lungs showed typical scar tissue formation characteristic of healed tuberculosis. The visceral layer of the pericardium was adherent throughout to the myocardium. The pericardial cavity was obliterated and contained no fluid. The parietal layer of the pericardium was adherent to both lungs and to the diaphragm and contained extensive calcification. Upon section the heart muscle showed marked fatty and parenchymatous degeneration. The liver was much enlarged and typical "nutmeg" in appearance with extensive fibrosis. The peritoneum was thickened and the abdominal cavity contained a moderate amount of ascitic fluid.

The Pathological Diagnosis was acute bronchopneumonia; chronic healed apical tuberculosis; chronic adhesive pericarditis with calcification; chronic myocarditis, chronic mediastinitis, chronic peritonitis with ascites; chronic congestion and cirrhosis of the liver with hypertrophy (the pseudocirrhosis of Pick).

Stereoscopic films of the excised heart (Fig. 3) showed an inverted Y-shaped area of calcification extending upward and posteriorly. The superior limb of the "Y" ended in an irregular area of calcification behind the aorta. There also was evident a dense area of calcification in the pericardium covering the left ventricle at the point of its contact, through adhesions, with the diaphragm.

TREATMENT

L. Brauer[20] first suggested in 1902 operative interference to relieve the heart burdened by adhesions. The operation consisted in the subperiosteal resection of the left fourth, fifth and sixth ribs, with their cartilages, extending from the midclavicular line or slightly beyond, to the sternum. The purpose of the operation was to allow greater freedom of movement for the heart's contractile efforts. The pericardial adhesions to the rigid chest wall have been believed by all who have studied the condition to be responsible for much of the cardiac operation upon the heart itself. A more appropriate descriptive term known, was, however, an unfortunate selection, since it implied an overwork. The term cardiolysis, by which the operation has become for the operation would be precordial costectomy.

It is remarkable that the operation as a means of relief has not attracted more attention. It does not involve great risk, and there should be little shock. It may be done under local and block novocaine or procaine anesthesia, a 0.5 per cent solution being employed. The anesthesia should include each intercostal nerve posterior to the portion of ribs to be excised. It has been customary to remove the periosteum of the fifth and sixth ribs, for about 1.5 inches to prevent regeneration of bone. Marvin and Harvey[21] in 1924 showed that the operation has been performed only thirty-four times. Twenty-eight of the operations were by Continental surgeons. Reports of the operation upon seven patients in the United States are available. These were reported by Dunn and Summers,[22] by Summers,[23] by Hirschfelder,[24] by Smith,[25] by Marvin and Harvey (loc. cit.), and by Cutler and Sosman (loc. cit.).

The relief obtained by many of the patients through the operation warrants its more common employment. The earlier the operation may be performed, before extensive damage has been done to the myocardium as a result of overwork, and before chronic pleuritis and chronic peritonitis have occurred, the better will be the outlook for the individual patient.

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STATISTICAL STUDIES BEARING ON PROBLEMS IN THE CLASSIFICATON OF HEART DISEASES

I. INTRODUCTION*

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THIS is the first of a series of statistical studies which the New York Heart Association designs to publish. There are urgent reasons for undertaking investigations of this character for they have an especial importance in considering programs dealing with the desire to improve the public health. The chief of these is practical and has for its object the effort to ascertain the significant aspects of this subject. We need to inquire: what is the state of knowledge in respect to etiology, to the natural history, to the therapeutics of these diseases? Are these phases of the problem in which there is hope of amelioration by one or another method? Are the methods which are available suitable to the requirements?

The inspection of curves of mortality statistics covering a succession of years has brought to light the fact that a continuous increase in the number of deaths due to heart and circulatory diseases is taking place. A flutter of excitement has in consequence taken place. In certain quarters, encouraged by the success which has attended the effort to check the number of deaths due to tuberculosis, the possibility has suggested itself by analogy, that similar success will in all probability attend the adoption of comparable methods in the case of heart disease. Before embarking on a program of activity having in view results such as might be promised on the basis of the experience with tuberculosis, it seemed wise to the Research Committee of this Association to explore the subject of the incidence and classification of heart disease as a whole.

To proceed in this manner seemed the better course, for certain differences between tuberculosis and heart disease exist which make proceeding on the basis of too close a similarity dangerous both to our thinking and to our hopes. In the general mind, tuberculosis means pulmonary tuberculosis; and no doubt, statistically this form of the disease overshadows the osseous, glandular, and intestinal forms. If this inference is correct a difference between heart disease and tuberculosis should be pointed out: tuberculosis is a single infection of one organ—the

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lungs; heart disease, on the other hand, includes a number of ailments representing quite different orders of disease. To be comparable, the object of study on the part of Public Health Associations should have been diseases of the lungs. In this group should have been included not only tuberculosis but lobar and bronchopneumonia, syphilis of the lungs, asthma, pneumonokoniosis, and terminal pneumonia. In diseases of the heart there are first, the infectious varieties, divisible at least into two separate groups—an acute one with which bacteria already known are associated, and "rheumatism", the cause of which remains undiscovered; syphilis is a third variety. Then there are the chronic forms, again of two sorts; first, those associated with the so-called degenerative diseases, such as arteriosclerosis, arterial hypertension, and Bright's disease, of which damage to the heart either is part and parcel of the general process or is a sequel to these changes, the damage in any case being associated with more general or extensive disease; and second, there are those alterations to the heart which occur in old age and may properly be called senescent. Whether this class is to be reckoned a disease appears still to be an open question; at all events heart failure in old age is a prolific source for disability. Finally there are large numbers of individuals who suffer from what are called neuroses—phases of disability which have nothing to do with alterations in structure of the heart, whether as sequels of infectious diseases or as forms of degeneration. For the moment it is unnecessary to deal with those other classes of heart affection; namely, congenital malformations and those associated with poisons as in the case of hyperthyroidism.

Does this rough classification have a meaning for the problem of prevention, in the same sense in which one may speak of prevention in the case of tuberculosis or of cancer? In order to prevent diseases there are at our disposal, where they are applicable, several procedures that may be adopted. Consider the case of typhoid fever. The bacterium that causes the disease is known. To prevent the disease, two methods are employed. Care is exercised so that the typhoid bacillus is not ingested either in water or milk or in other food. Another method which is used is that of vaccination. Both these procedures require that something of the bacterium which causes the disease be known; either cultivation of the bacilli must be possible or in the absence of the discovery of the organism, one or more of its significant habits must be understood so that it may be dealt with in an indirect fashion as in yellow fever. Without going further into matters of this nature it becomes clear that in the case of rheumatic fever we possess neither of these advantages. The etiological organism is unknown, its life habits are unknown, its progress into the body cannot be intercepted. One cannot now be saved from the disease by any means based on the practices of bacteriology or immunity.

There are still two other methods of procedure; we may either shut to the infecting organism a supposititious portal of entry to the body, such

as the pharyngeal tonsils, by excising them, or we may institute measures of isolation, such as are employed in the contagious diseases. The usefulness of the former of these methods has been studied, but still requires, in order to be on safe ground, more detailed and more critical analysis in larger numbers of cases than has yet been attempted. The second method has been less studied; it is important to pursue it, but to appraise the value of the data which are obtained requires the exercise of vigorous critical judgment.

Of treatment of the rheumatic form of heart diseases nothing need for the moment be said; no approach to a knowledge of how to arrest or to change its course is known. Cures, when they occur, are spontaneous, and so far do not fall within the province of rational therapeutics. All of this creates a difficult situation; it is difficult not because we are without hope, but only because for the moment we are ignorant and powerless. The difficulties are not insuperable, they need, however, to be understood and to be defined. In many quarters the effort to solve them continues to be made sedulously.

When we turn, however, to the chronic diseases, especially of the senescent types, have we reason to look forward to the possibility of comparable relief, that is to say, of prevention or of the delay of their onset? The answer in the first case, is naturally "No". In the second, no doubt, much may be accomplished. Here we deal with inevitable, not accidental, forces of nature. Relief in the sense of amelioration of discomfort may be, indeed is, possible; but prevention and cure are obviously not. Is the realization of this situation important? Does the number of cases, the chronic cases involved, form a significant part of the total? In the report of Dr. Wykoff and Miss Lingg now published it appears clearly that cases of this group form no inconsiderable number. When the statistics come to be analyzed further it may indeed appear that the *increasing* rate of deaths actually takes place in this group, and not in the infectious ones in which the possibility of prevention and cure remains open.

On all sides have been heard statements to the effect that the death rate in the past fifty years has been decreasing. To make statements like this is to prepare the way for disillusion. Surely 100 per cent of people die; at certain periods, coincident with certain events or the introduction of certain procedures and arrangements, the rate may fall. But for the fall there must at some time be compensation, until a new equilibrium is established. If deaths are obviated in infancy or early adult life, they must take place in the later decades. The duration of life, its expectancy, as we learn from actuaries has in fact increased. Does not the situation amount to this? We have been saved from death in youth, to live, it may be, laborious days, and to die in the end by more lingering mechanisms.

We must learn as the result of these statistical studies the nature of the changes from the point of view just discussed, that are taking place in the life of the community. No doubt we shall learn much from the changes in shape of specific death rate curves.* We must study whether, if these changes have occurred, they have occurred as the result of efforts at prevention of infectious heart disease in early life or for causes related to the saving of life at other decades and from other diseases. We must learn what percentage (whether the number of cases remains stationary or increases or decreases) is prevented, what percentage cured, what percentage senescent. Only by analyses such as these shall we learn the nature of the problem with which we must deal, and on what aspect of it is the major emphasis most intelligently to be placed.

There are many other problems for which our methods may yield solutions: studies in the natural history of these diseases; their duration, and whether this is modified, and how much, by differences in social and economic environment; does symptomatology vary with class and with age; what is the bearing of age on the possibility of recovery; what influences are exerted on their course by treatment; of what use are certain forms of treatment, such as rest, work, homes for convalescent patients, operations on portals of entry, such as the teeth and tonsils. These are all ancient but still vital questions which continue to await suitable answers until comprehensive statistics compiled from the viewpoint of clinical medicine become available. To compile such statistics with the purpose of seeking answers to these questions is the object of the inquiries which the Research Committee of the New York Heart Association has set itself. On the answers depends the question of what is significant in morbidity. On these answers may very well depend the direction experimental research is to take. But there is also another direction in which study is important. Here we are concerned rather with the systematic observation of the symptoms and signs of disease, in the patient himself either in the clinic or at the bedside. This in itself is today an essential part of research. From this study we hope to learn what further effort is required in the proper understanding of the pathological processes which are involved and of bringing to these appropriate relief.

Our object therefore is twofold, nosological and experimental; nosological, in the interests of our understanding of natural events, with the view to making appropriate provision for each class of disease; experimental, in the same interests but further in an attempt to define what is required in rational therapeutics. To us it seems that our methods are full of promise.

*Specific death rate curves fractionate the familiar rate curves into age periods. A point on the curve represents the ratio of deaths at a given age period to the population alive at that age period.

II. ETIOLOGY IN ORGANIC HEART DISEASE*

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INTRODUCTION

THE figures for the United States Registration Area and for the Industrial Policy Holders of the Metropolitan Life Insurance Company represent the mortality rate of organic heart disease as a curve rising with each advancing age group. The proportion of deaths under the age of forty years is relatively small. The significance of the death rate under the age of forty years is brought out only when the toll exacted by heart disease is compared with that exacted by other diseases in these early age groups.[1] These facts, together with the results of the physical examinations of the draft, of applicants for life insurance, of the food handlers of New York City, garment workers, and school children of New York City, and elsewhere, which form the basis of the general estimate that approximately 2 per cent of the population of the United States is afflicted with organic heart disease,[2] have led the New York Heart Association to attempt to answer the question: What is the morbidity of organic heart disease, or, how many people are actually suffering from organic heart disease and what is the incidence of the disease by age groups?† This question and that of the cause of the disease, its duration, and the effect of social environment, economic conditions, and therapeutic measures on the course of the disease, must be answered before any appreciable advance can be made in studying the measures which can be taken in the attempt to bring relief from this group of diseases. Since heart disease, unlike tuberculosis, is not a reportable disease, and the recording of facts that might lead to enlightenment cannot be enforced, these questions are difficult to answer. The obtaining of this information the New York Heart Association considers one of its important functions. To this end, it has regarded the collection of data in a statistical form as advisable. In order that the information when obtained may serve this purpose, special charts have been devised which have been recommended for use in cardiac clinics.[3] As the need for treatment by a specialist in heart disease becomes increasingly felt, and as more and more cardiac patients are referred to cardiac clinics, it is

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†It has been pointed out by A. E. Cohn (Nels. Loose-Leaf Med., 1921, iv, p. 267: Etiology of Chronic Diseases of the Heart) that even under most favorable conditions for reporting the occurrence of the disease, the actual morbidity could not be ascertained on account of the insidious nature of the onset of the disease, which makes its recognition difficult and often delayed for many years. Nevertheless, the age distribution of cases that are recognizable should be of value.

hoped that by such means may be gathered adequate information, accurately defined and uniformly described, so that statistical analyses may be made along the lines suggested.

The following discussion is a preliminary study of the first thousand cases which have been recorded on these charts. Owing to the successful results in the use of the charts in a clinical system suitably organized, we are encouraged in the belief that the future success of collecting data on the subject of organic heart disease is assured. After a somewhat tedious transition period from a simpler form of record, previously employed in the clinic, to the new form, it was found that the use of the charts increases rather than decreases the efficiency of the clinic. In fact, after two years' experience, it is our opinion that the provisions made in the chart for recording facts exactly, in the form of a code rather than in the form of a narrative and diagrammatic description, has made it possible (1) to spend more time on the patient and less on the record, while at the same time the important points revealed by the examination have been completely recorded; (2) to see more patients at each session than would otherwise have been possible, and (3) to collate the experience obtained for study and analysis with a minimum expenditure of time and effort.

PLAN OF STUDY

To attempt to answer the following questions was the aim of this preliminary study:

1. What are the forms of heart disease, from the point of view of etiology, that are found among adults, and what is their age and sex distribution?

2. Do sex, age, race, or nationality bear any relation to the type of heart disease?

THE SAMPLE, SIZE, AND REPRESENTATIVENESS

It was necessary, in the first instance, to select from all the material available a group of patients so managed that it serve the purpose in view. The group studied obviously cannot be taken as completely representative of all cardiac patients. It was necessary, therefore, to learn how far it formed a suitable sample. The sample consists of 1001 cases of which 85.4 per cent are among clinic patients and 14.6 per cent among private patients.* If we assume that the estimate is correct which places the morbidity rate of organic heart disease at 2 per cent of the total population of the United States, and apply this ratio to New York City, the number afflicted should be 112,400. Of this number, the sample studied (1001 cases) is 0.89 per cent. But since the cases studied are chiefly

*The Standard Cardiac Charts were used for recording the histories of the private as well as the public patients. The private patients studied were in the practice of John Wyckoff, M.D.

adult, they may be taken to constitute 1.3 per cent of the adult cardiac population.* Whether, in point of fact, the sample is representative of the cardiac population of New York City cannot be ascertained, since the number of the afflicted is merely estimated and nothing of its constitution is known. If we could increase the size of the sample to several hundreds of thousands, or, if we could make corroborative studies and find similar results, we should conclude that our sample was representative and draw inferences from an analysis of our data. Until this is done, we merely assume that this sample is representative.

MORTALITY AND MORBIDITY

Age Distribution.—If one studies the mortality curve of organic heart disease in New York City from 1920 to 1923† (Fig. 1), one is at once impressed with the fact that beginning with the third decade the curve rises, and continues to do so until it reaches its highest point in the seventh decade, and remains high in the eighth decade. The morbidity curve for the public patients is highest in the third decade, reaches a second mode in the fifth decade, begins to fall in the sixth decade, and then descends rapidly. The morbidity curve for the private patients, although it more closely approximates the mortality curve, reaches its maximum point in the sixth decade, is still high in the seventh, and thereafter falls almost as precipitously as does the curve for public patients. The first part of the morbidity curves is approximately the same for both morbidity groups of patients, the rate being as much higher in the third than in the second and fourth decades for the group of public patients as for that of the private patients.

In studying the second part of the curves the following questions present themselves at once:

1. Why, when the death rate is highest in the seventh and eighth decades, is the morbidity rate highest one or two decades earlier?

2. Why do we apparently have the maximum incidence of heart disease in the fifth decade among public patients, and in the sixth decade, ten years later, among private patients? Does this mean that under greater economic strain patients die from ten to twenty years earlier?

The morbidity curve of public patients (Fig. 1) begins to fall at the end of the 40-49 year period, twenty years before the mortality curve falls; that of the private patients at the end of the 50-59 year period, ten years before the fall in the mortality curve. Why this is so, is unknown, but the following explanations may be offered.

In the first place, it may be that because of the severity of their symptoms, patients in the higher age groups are too ill to be ambulatory and

*The cases studied, fifteen years of age and over, number 966. The population of N. Y. C. fifteen years of age and over in 1920 was 3,796,127 (N. Y. C. Census Committee 1920). The age given, in each case, is the age of the patient when admitted to the clinic, not necessarily the age at onset of the disease.

†From figures of Bureau of Records, Department of Health, New York City.

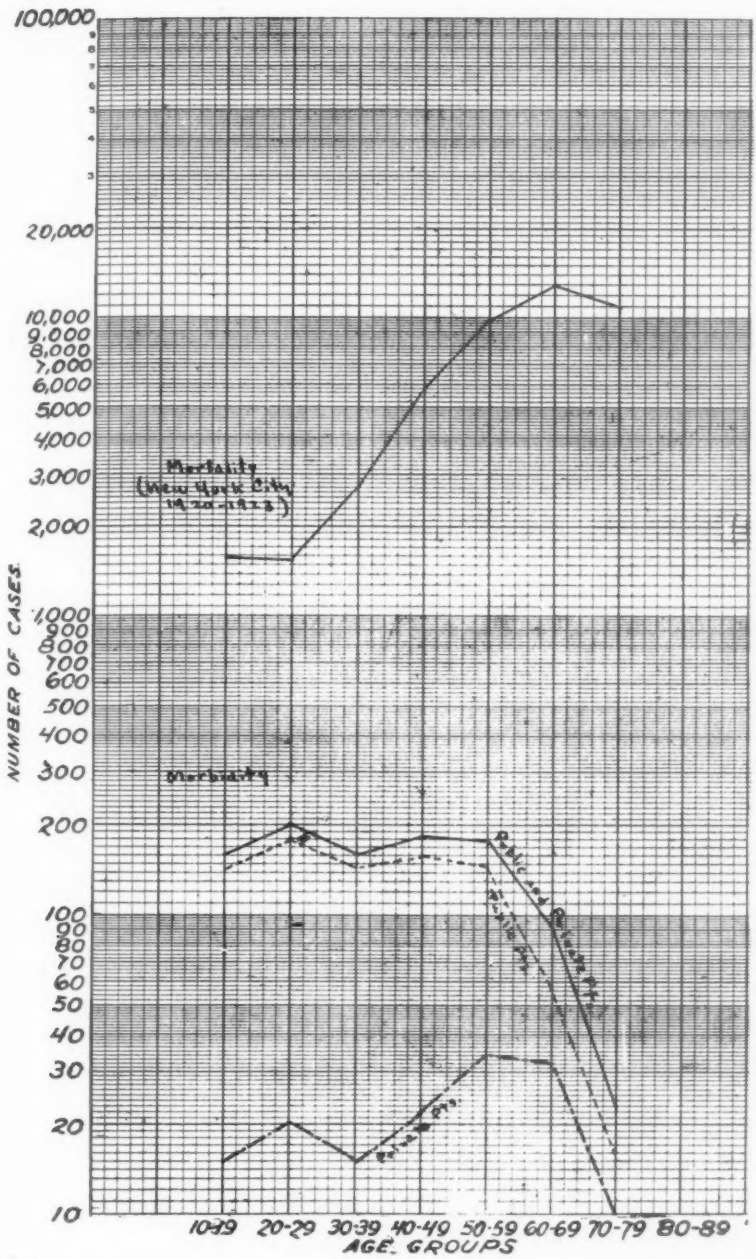

Fig. 1.—Organic heart disease by age groups. Morbidity and mortality.

have therefore escaped observation in this sample. But this is an explanation only in part. As a matter of general experience one knows that elderly patients with heart failure do not remain in Class III* for nearly so long a time as ten years. If they die in such large numbers after the age of sixty years, they must, therefore, be ambulatory patients. This low morbidity rate is in all likelihood to be explained, rather, by the probability that in the upper age groups general physical degeneration is accepted by individuals with more or less resignation, and that owing to the insidious nature of arteriosclerotic heart disease, which is the type of disease most commonly found among elderly people, the cardiac condition is not recognized by the patients as cardiac but is accepted as part of senile weakness for which quite naturally they do not seek relief. Furthermore, the results of treatment are known to be less satisfactory on account of the general senile degeneration at the ages in which arteriosclerosis is prevalent; the effort of attending the clinic or consulting the private physician is greater; economic pressure is no longer so insistent a motive for requiring relief, since at these age groups patients have ceased to work either in part or whole. They are, indeed, not infrequently supported by their children.

We come now to the second question: Why does the curve of morbidity of the public patients begin finally to fall a decade earlier than that of the private patients? At first glance, it might seem that public patients die ten years earlier, before they reach the age of sixty, on account of less favorable economic conditions. This explanation is however not adequate, because, although the proportion of public to private patients in the general population is not known, surely the latter are not numerous enough to account for the great number of deaths reported after the age of fifty-nine, which would have to be the case if it were true that the expectancy of life is less by about ten years among public patients.

The difference in these curves is rather to be explained by the probability that public patients above the age of fifty-nine have escaped observation in this sample. Public patients, so-called, seek medical aid not only from medical clinics but also from physicians in private practice. Physical examinations are frequently superficial and the presence of arteriosclerotic heart disease often escapes detection until failure is present. The patient then tends to become a bed rather than an ambulatory

*This refers to functional capacity as classified by the New York Heart Association:

Class I Patients with organic disease, but able to carry on ordinary physical activity.

Class II Patients with organic disease, but unable to carry on ordinary physical activity.

a. Activity slightly limited.

b. Activity greatly limited.

Class III Patients with organic heart disease, with symptoms of heart failure at rest.

case. So far as the patients are concerned, the onset and course of the disability is so slow and insidious that attention is not directed to the heart as the cause of the difficulty. In the group of private patients, on the other hand, diagnoses are probably more accurately made and recommendations for treatment more successfully carried out. The point may be made that differences similar to these obtain also in the younger age groups. We believe, however, that this is not the case. Heart disease occurring before the age of forty years, as will be shown later, is chiefly rheumatic. In many cases, there will have been one or more attacks of active rheumatic heart disease during which heart failure may have occurred. Such an illness makes a profound impression not only on the family of the patient, but on the patient as well, so that even among the less intelligent and the poor every effort is made to secure expert advice.

If then, the arteriosclerotic form of heart disease is not recognized until failure is present, and the patients become bed rather than ambula-

TABLE I

FUNCTIONAL CLASSIFICATION OF PUBLIC AND PRIVATE PATIENTS

FUNCTIONAL CLASSIFICATION	AGE GROUPS							
	50-79 YEARS				10-79 YEARS			
	PUBLIC PATIENTS		PRIVATE PATIENTS		PUBLIC PATIENTS		PRIVATE PATIENTS	
	NO.	%	NO.	%	NO.	%	NO.	%
Class I	7	2.8	0	—	103	11.4	15	10.3
Class II	182	73.1	42	55.2	633	69.9	75	51.4
Class III	59	23.7	34	44.7	162	17.9	56	38.3
No Report	1	0.4	0	—	7	0.7	0	—
Total	249	100.0	76	100.0	905	100.0	146	100.0
Totals		325	30.9%			1051	100.0%	

tory cases, a study by ten year age groups of bed cases should throw light on the decades at which arteriosclerotic heart failure is predominant. The records of 695* successive admissions to the wards of the third medical (N. Y. U.) division of Bellevue Hospital were accordingly analyzed. On examining the curve representing these cases (Fig. 2) it will be seen that the greatest incidence of heart disease in this group occurred in the sixth decade and that the curve in this portion is similar to the private patient morbidity curve. Furthermore, while only 17.9 per cent of the total clinic patient group are in Class III (Table I), 38.3 per cent of the total private patient group are in this class; between the ages of fifty and seventy-nine 44.7 per cent of the private and only 23.7 per cent of the clinic patients are in Class III. That is to say, among the patients whose economic resources enable them to be spared physical exertions and hardships, a considerable number appear to remain ambulatory, while others appear to become ward cases. The dif-

*These cases are not included in the original sample of 1001.

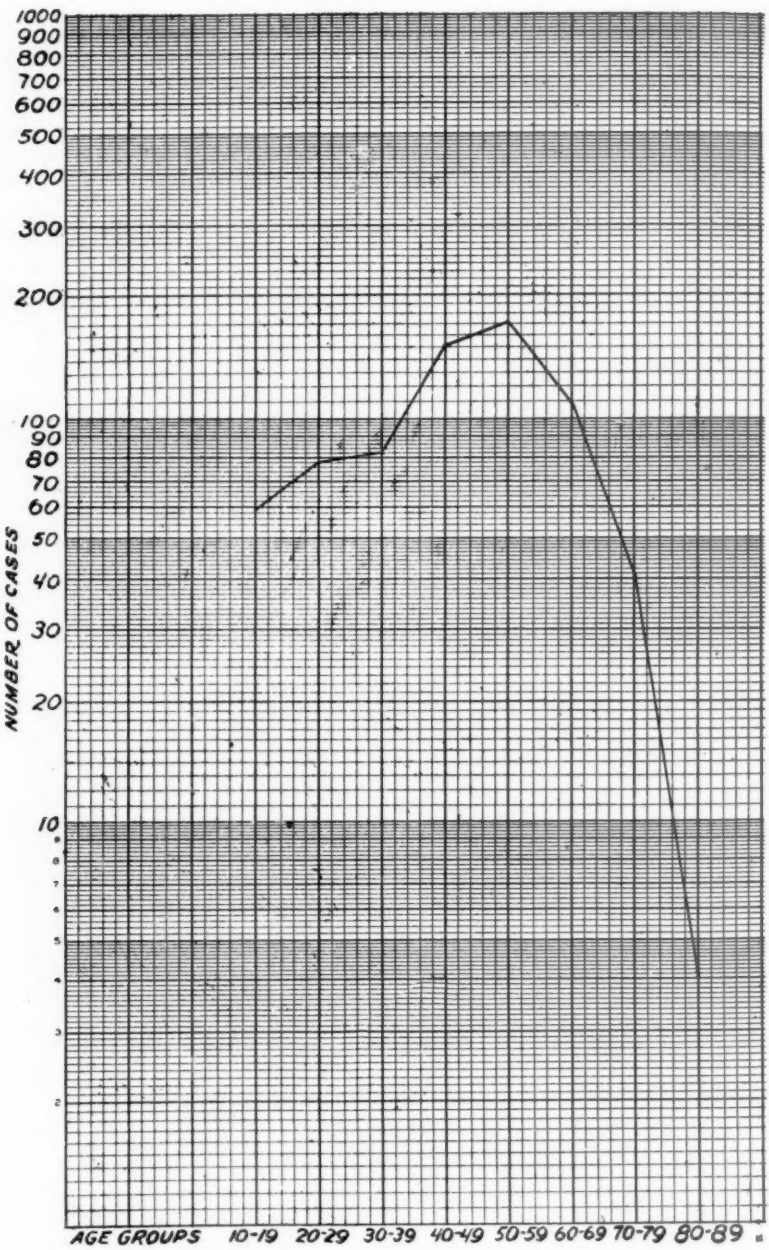

Fig. 2.—Incidence by age groups of ward cases of organic heart disease.

ference in reaction to the condition accounts in large measure for the divergence in the morbidity curves we have shown for the public and private patient groups.

It should be noted that it is the ward patient curve (Fig. 2) which corresponds the more nearly with the mortality curve (Fig. 1). This is what should have been expected. It does not, however, correspond with it exactly. The mortality curve reaches its highest point in the seventh decade, the ward patient curve does so ten years earlier; and, while the eighth decade is the second highest point in the mortality curve, in the ward patient curve the rate for the eighth decade is lower than for any preceding decade. Why the morbidity rate among cardiacs

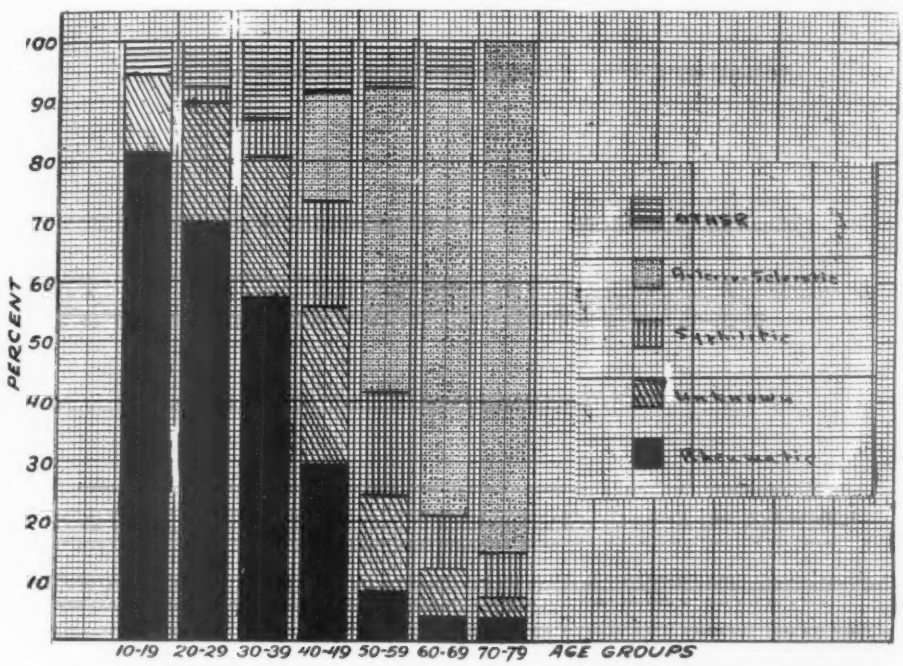

Fig. 3.—Incidence of organic heart disease arranged by age groups and etiological types.

should fall so abruptly in a general medical service, such as that in Bellevue Hospital, when the mortality rate for the city remains so high is hard to understand.

Returning now to the mortality and total morbidity curves, we find further dissimilarity in the curves in the earlier decades. The morbidity curve is a distinctly bimodal curve. Therefore, it is necessary, at this point, to consider the various types of heart disease which make up each of the groups studied and their respective relations to each of the curves.

During the second, third, and fourth decades, the great majority of patients suffer from rheumatic heart disease and from heart disease of unknown origin (Fig. 3). The latter group, as we shall point out, we believe to be chiefly rheumatic. At first, the morbidity from heart dis-

case (Fig. 1) seems to be as great in the second, third, and fourth decades as in the fifth, sixth, and seventh decades, or even greater. As a result of comparing the morbidity with the mortality curve during these decades one might be led to conclude that patients suffering from rheumatic heart disease live a considerable number of years, the majority dying after the fourth decade; and that the rapid rise in the mortality rate during the fifth, sixth, and seventh decades is due, in large part, to deaths from rheumatic heart disease. If one studies separately the curves of the clinic and private cases and of the ward patient group, however, one sees at once that this is not the correct explanation. Among both the private patients and the ward patients only about one-third of all cardiac cases occur between the ages ten and thirty-nine, whereas two-thirds are found between the ages forty and forty-nine, Among the clinic patients, on the other hand, over half of all the cases occur before the age thirty-nine and less than one-half between the ages forty and forty-nine. One might now be led to suppose that among public patients rheumatic heart disease is more prevalent than among private patients, and also that it is a greater cause of total cardiac morbidity than arteriosclerotic heart disease, which is obviously the greatest cause of morbidity during the fifth, sixth, and seventh decades. This conclusion is, however, not borne out by a comparison of the morbidity rates by age groups of the clinic patient group with those of the ward patient group, which two groups are socially similar. A glance at this curve (Fig. 2) shows that it follows the private patient curve fairly well.

For twelve years the practice has been followed of referring cardiac patients, both adults and children, to the cardiac clinic. As children reach the age of fourteen years in the children's cardiac clinic they are graduated to the adult cardiac clinic. Cases of rheumatic heart disease are therefore received from three sources within the hospital; the ward service, the children's cardiac clinic, and the general out-patient department. The last group is received chiefly from the obstetrical and prenatal clinics, practically all cases exhibiting rheumatic heart disease, and from the general medical clinic. It has been noticeable that from the general medical clinic a majority of the cases referred have been cases of rheumatic heart disease. We receive patients also from outside sources, such as public schools and various social agencies. Of the public school children practically all have rheumatic heart disease, and the majority of patients referred from social agencies are sent to us with disease of this type.

These explanations, added to the points brought out above by a comparison of the various curves so far as the upper age groups are concerned, lead us to believe that the morbidity curve of the clinic group is not a true sample of cardiac morbidity as a whole; that it exhibits the proportion of cases in the younger age groups as being larger, while that in the older age groups appears to be smaller than the facts probably

warrant; that as regards age distribution, the private patient group and the ward patient group more nearly approximate what constitutes a representative sample.

RACE, NATIVITY, AND NATIONALITY

Of the 1000 patients that comprise our sample, 37, or 3.5 per cent, were colored. Sixty-four and one-tenth per cent were either foreign-born or native-born with one or both parents foreign-born (Table II). The foreign-born make up almost half of the total number of white patients (44.6 per cent). The percentage of what might be called American (at least two generations American), is only 13.9 (Table III). As would be expected, the proportion of native-born of native parentage is greater and that of foreign-born smaller among the private than among

TABLE II

TYPES OF ORGANIC HEART DISEASE CLASSIFIED BY RACE AND NATIONALITY

NATIONALITY			TYPE OF ORGANIC HEART DISEASE									
			TOTAL		RHEUMATIC		SYPHILITIC		ARTERIO-SCLEROTIC		OTHER	
			NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
White	Native-born											
	Native parentage*		341	32.4	139	30.9	24	26.3	64	27.3	113	40.8
	Foreign-born or native-born with foreign or mixed parentage	Italian	107	10.2	63	14.0	7	7.7	7	3.0	30	10.83
		Irish	208	19.8	72	16.0	21	23.1	68	29.1	47	16.96
		German	72	6.8	22	4.9	10	11.0	26	11.1	14	5.06
		Hebrew	152	14.5	72	16.0	4	4.4	35	15.0	41	14.8
		Other	135	12.8	65	14.2	14	15.4	30	12.8	26	9.38
		Total	674	64.1	294	65.1	56	61.6	166	72.7	158	57.05
Colored			37	3.5	16	3.6	11	12.1	4	1.7	6	2.17
Total			1051	100.0	449	100.0	91	100.0	234	100.0	277	100.0

*This group includes native-born whose parentage was not recorded.

TABLE III

DISTRIBUTION OF WHITE PATIENTS ACCORDING TO NATIVITY

NATIVITY		NUMBER	PER CENT
Native-born	Native parentage	135	13.9
	Mixed parentage	38	3.1
	Foreign parentage	204	21.1
	Parentage unknown	153	15.7
Foreign-born		432	44.6
No Report		6	0.6
Total		958	100.0

the public patients. In the public patient group the foreign-born constitute 44.4 per cent of the total number of patients, and the native-born of foreign or mixed parentage about 25.0 per cent.

Sir Arthur Newsholme[4] has pointed out that in England there has for several decades been an almost continuous fall in the total death rate, affecting middle and advanced as well as early life, and that the death rate at ages over forty-five in the United States is still slightly increasing beyond what it was eleven years ago. Dr. Dublin[5] found that the high death rate in this country in the higher decades is from six to seven times greater among immigrants than among native-born; indeed,

the rate is higher than it is at home. If, as is generally supposed, the conditions of life are better in the United States, this is not the result we might expect. A curious experience on our part is the fact that although the death rate is so high, we do not, at least at the Bellevue clinic where we might properly expect them, meet with this class of people.

Of the foreign-born or native-born of foreign or mixed parentage, about one-third were Irish, about one-sixth Italian, not quite one-fourth Hebrew (of whom more than half were Russian, and about one-fourth Austrian), and about one-tenth German (Table II). Whether there is present in the morbidity of organic heart disease any factor such as racial immunity, as is believed to be the case in tuberculosis, cannot be learned from the data here available. We shall consider the question again in connection with the various types of heart disease, especially the infectious varieties.

TABLE IV

CASES OF ORGANIC HEART DISEASE ARRANGED ACCORDING TO SEX, IN THE EXPERIENCE OF VARIOUS OBSERVERS

OBSERVER	NUMBER OF CASES	MALES %	FEMALES %
Kostler[1] (1883)	116	52.5	47.5
Bamberger[1]	211	51.3	48.7
Duchek[1]	–	41.0	59.0
Leuch[1]	67	48.6	51.4
Willok[1]	–	38.0	62.0
Fatianoff[1]	–	41.0	59.0
Andrew[2]	1494	39.8	60.1
Wyckoff	1001	60.2	39.8

[1]Gerhardt, D.: Herzklappenfehler, Wurzburg, 1913.
[2]Norris, G. W.: Studies in Cardiac Pathology, Philadelphia, 1911.

SEX DISTRIBUTION

Slight and insignificant differences for the two sexes appear in the death rate for organic heart disease. The figures for the United States Registration Area[6] show the rate to be slightly higher in males except in the first three and in the ninth decades; in these it is higher in females. The figures published by the Metropolitan Life Insurance Company for the Industrial Policy Holders show the rate to be slightly higher in females up to and including the ages twenty to twenty-four, and after that higher in males. The greater death rate in females than in males in early adult life is similar to what has been found in the tuberculosis mortality rates, but for the fact that it is much more pronounced in the latter.

The experience of various observers seems to vary with regard to the distribution of the morbidity of organic heart disease between the sexes. In our series slightly less than two-thirds of the patients were males, and slightly more than one-third females (Table IV). The proportion of the sexes is the same in both public and private patients. The rate is higher in females in the second and the third, or chief child-bearing decades,

and very much higher in males in all other decades (Table V). Among the public patients the rate is highest in males in the sixth and seventh decades, and in females in the fifth as well as the third decade. Any attempt at explaining these differences is unsatisfactory without an analysis of the various types of heart disease that make up the curve as a whole, and the incidence of sex for age groups as related to these types. We shall, therefore, consider the sex incidence for the different types in the appropriate place.

TABLE V

INCIDENCE OF ORGANIC HEART DISEASE ARRANGED BY SEX, AGE GROUPS, AND ETIOLOGICAL TYPES

	AGE GROUPS	TOTAL		ETIOLOGICAL TYPE									
				RHEUMATIC		UNKNOWN		SYPHILITIC		ARTERIO-SCLEROTIC		OTHER	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Males	10-19	88	13.8	71	30.8	11	10.4	0	0	0	0	6	12.5
	20-29	93	14.5	62	26.9	19	17.9	4	5.0	0	0	8	16.7
	30-39	89	13.9	52	22.6	22	20.8	9	11.2	1	0.5	5	10.4
	40-49	120	18.7	31	13.5	31	29.2	25	31.2	21	12.1	12	25.0
	50-59	143	22.4	10	4.3	18	17.0	31	38.7	73	42.1	11	22.9
	60-69	78	12.2	3	1.3	4	3.8	9	11.2	56	32.1	6	12.5
	70-79	27	4.2	1	0.4	1	0.9	2	2.5	23	13.2	0	0
	Total	639	100.0	230	100.0	106	100.0	80	100.0	174	100.0	48	100.0
Females	10-19	75	18.2	62	28.3	10	12.3	0	0	0	0	3	7.1
	20-29	112	27.2	81	37.0	23	28.4	0	0	0	0	8	19.0
	30-39	81	19.6	46	21.0	17	20.9	2	18.2	0	0	16	38.0
	40-49	68	16.4	23	10.5	17	20.9	7	63.6	12	20.0	9	21.4
	50-59	53	12.8	6	2.7	12	14.8	2	18.2	29	48.3	4	9.5
	60-69	23	5.5	1	0.5	2	2.5	0	0	18	20.0	2	4.8
	70-79	1	0.2	0	0	0	0	0	0	1	1.9	0	0
	Total	413	100.0	219	100.0	81	100.0	11	100.0	60	100.0	42	100.0
Both Sexes	10-19	163	15.5	133	29.6	21	11.2	0	0	0	0	9	10.0
	20-29	205	19.5	143	31.8	42	22.5	4	4.3	0	0	16	17.8
	30-39	170	16.1	98	21.8	39	20.8	11	12.0	1	0.4	21	23.3
	40-49	188	17.8	54	12.0	48	25.7	32	35.1	33	14.1	21	23.3
	50-59	196	18.6	16	3.6	30	16.0	33	36.2	102	43.6	15	16.7
	60-69	101	9.5	4	0.9	6	3.2	9	10.0	74	31.6	8	8.9
	70-79	28	2.5	1	0.2	1	0.5	2	2.1	24	10.2	0	0
	Total	1051	100.0	449	100.0	187	100.0	91	100.0	234	100.0	90	100.0

ETIOLOGICAL TYPES

As was pointed out in the early part of this paper the cases of rheumatic and unknown etiology comprise for the most part the earlier age groups, and cases of arteriosclerotic etiology the latter age groups (Fig. 3, Table V). Among the public patients, moreover, more than 50 per cent are drawn from the younger ages, and are affected by heart disease of rheumatic or unknown etiology; 30 per cent are drawn from the older age groups and represent largely arteriosclerotic disease. There is great similarity between the private and ward cases not only in the age, as was earlier pointed out, but also in the etiological distribution, the rheumatic cases constituting about 25 per cent, the arteriosclerotic about 40 per cent (Fig. 5, Table VI). The prolongation of life within the last years is coincident with the increase in mortality and morbidity

TABLE VI

DISTRIBUTION OF ETIOLOGICAL TYPES OF HEART DISEASE IN THE DIFFERENT GROUPS

GROUP	TOTAL		ETIOLOGY									
			RHEUMATIC		UNKNOWN		SYPHILITIC		ARTERIO-SCLEROTIC		OTHER	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Total sample	1051*	100.	449	42.7	187	17.8	91	8.6	234	22.2	90	8.6
Public patients	890	100.	408	45.8	174	19.5	83	9.3	164	18.4	61	6.6
Private patients	161	100.	41	25.5	13	8.1	8	5.0	70	43.5	29	18.0
Ward patients	695	100.	188	27.0	123	17.7	65	9.3	276	39.7	43	6.2

*In several cases there were two etiological factors involved. In order to treat each of these, statistically, without increasing the groupings, each of the etiological factors was considered as an incidence of heart disease, making the total incidence 1051. For example, both rheumatic and syphilitic etiologies occurred in 11 cases, giving an incidence of rheumatic heart disease in 11 cases, and of syphilitic heart disease in 11 cases, or a total incidence of 22. Both rheumatic and arteriosclerotic etiologies occurred in 10 cases; syphilitic and arteriosclerotic in 5 cases; syphilitic and unknown etiologies in 2 cases, etc.

TABLE VII*

CASES OF ORGANIC HEART DISEASE ARRANGED ACCORDING TO ETIOLOGY, IN THE EXPERIENCE OF VARIOUS OBSERVERS

OBSERVER	NUMBER OF CASES	ETIOLOGY			
		RHEUMATIC	SYPHILITIC	ARTERIO-SCLEROTIC	UNKNOWN
		%	%	%	%
Mengel (Leipzig) 1896	670	59.2	rare	12.3	25.
Fatianoff (Basel) 1910	–	46.7 1.8 chorea	0.2	13.7	23.9
Gerhardt (Basel-Wurtzburg) 1913	300	64.3 1.6 chorea	4.7	9.7	12.0
Leuch (Zurich)	–	65.0			
Schmidt (Jena)	–	36.5			
St. Bartholomew's Hospital (Horder)	150	48.0	1.3		53.
Christiania	242	46.5	9.2		
Litten	400	35.0			30.0
Aldmuhler 1919	462	50.4	1.8	3.7	14.9

*Gerhardt, D.: Herzklappenfehler, Wurzburg, 1913.
Norris, G. W.: Studies in Cardiac Pathology, Philadelphia, 1911.
Cohn, A. E.: Etiology of Chronic Diseases of the Heart, Nels. Loose-Leaf Med., 1921, iv, 267.

rates for degenerative diseases, among them arteriosclerotic heart disease. It seems, therefore, that the private patient as well as the ward patient series is more representative than the clinic patient series with regard to the distribution of etiology as well as the age distribution.

It is interesting to note that in the experiences of other observers the percentage classified as rheumatic, which we consider approximately equivalent to the younger age groups, is similar to our experience in the clinic patient group (Table VII). It must be remembered, however, that our sample is limited to adult patients, while most of those here tabulated include children. This fact would, of course, make the proportion of rheumatic cases in their series somewhat larger than our own. Whether any attempt has been made to account for the relation of these figures to the mortality rates in the respective countries which corre-

spond in general to those in our own country, as we attempted to do in the first part of this paper, we do not know. Since the number of cases recorded by each observer is less than 1000, it is probable that the small number of cases make the data unsatisfactory so far as the distribution of etiological types is concerned.

RHEUMATIC HEART DISEASE

Definition.—Under rheumatic heart disease were included cases that presented a structural lesion typical of the disease, with a definite history of one or more attacks of rheumatic fever in which acute joint involvement was present, or chorea, or two or more severe attacks of tonsillitis. In thirteen, or 2.9 per cent, of the cases a definite and prolonged history of "growing pains" or joint pains was the only etiological factor (Table VIII).

TABLE VIII

INCIDENCE OF RHEUMATIC HEART DISEASE CLASSIFIED BY SEX AND TYPE OF INFECTION

TYPE OF INFECTION	MALES		FEMALES		BOTH SEXES		
	NO.	%	NO.	%	NO.	%	PER CENT OF TOTAL
Acute rheumatic fever	149	55.6	119	44.4	268	100.	59.7
Chorea	9	32.1	19	67.8	28	100.	6.2
Tonsillitis	26	45.6	31	54.4	57	100.	12.7
Growing pains or joint pains	5	38.5	8	61.5	13	100.	2.9
Acute rheumatic fever and chorea	6	46.1	7	53.8	13	100.	2.9
Acute rheumatic fever and tonsillitis	25	62.5	15	37.5	40	100.	8.9
Acute rheumatic fever, chorea, and tonsillitis	5	35.7	8	61.5	13	100.	2.9
Acute rheumatic fever, and growing or joint pains	0		1	100.0	1	100.	0.2
Chorea and tonsillitis	0		4	100.0	4	100.	0.9
Chorea and growing or joint pains	0		1	100.0	1	100.	0.2
Acute rheumatic fever and chorea and growing or joint pains	0		1	100.0	1	100.	0.2
Tonsillitis and growing pains	2	33.3	4	66.7	6	100.	1.3
Type of infection not specified	3	75.0	1	25.0	4	100.	0.9
Total	230		219		449		100.0

Infectious Diseases.—Among the 449 cases that presented rheumatic etiology, the causative factor in three-fourths of the cases, or 74.8 per cent, was rheumatic fever, either alone or in combination with other infections (Table VIII). This was found to occur almost equally in the sexes, slightly more in males (80.4 per cent) than in females (68.4 per cent). Tonsillitis was a causative factor in 26.7 per cent of the total in 13.3 per cent and "growing" or joint pains in 4.8 per cent. In the two latter categories the incidence was more than twice as cases. In the two latter categories the incidence was more than twice as high in females as in males. Rheumatic fever alone, was responsible for 59.7 per cent of the cases, tonsillitis alone for 12.7 per cent rheumatic

fever and tonsillitis for 8.9 per cent and chorea alone for 6.2 per cent of the cases. Here again we find that except in the case of chorea, which was found to have occurred, alone, twice as many times among females as males, there seems to be no great difference in the sexes. This is consistent with the comment which has frequently been made, especially by pediatricians, on the greater frequency of chorea among girls than boys.

Age.—The marked similarity in the incidence of rheumatic heart disease by age groups, for the whole sample, the clinic and private patient groups, separately, and the ward patient group is striking (Table VI). More than 95.2 per cent of the cases occur in the ages below fifty in the total clinic and ward patient groups, and 90.3 per cent in these ages in the private patient group. The number increases in the third decade in which we find the largest proportion of cases, in each of the three groups, and then decreases with each advancing decade. This is consistent with the experience of other observers (Table IX). It agrees, furthermore, with previous findings that rheumatic fever is rare after the age of thirty or forty, and that when it occurs, the probability of cardiac involvement is greatly diminished.[7] Further analysis of the data available in this connection shows that the increase in the proportion of cases in the third decade is true only in the case of females (Table V). When we compare the clinic and private patient groups, we find that the proportions of cases in the early decades are almost identical (Fig. 5), differing only by a fraction of 1 per cent. The rates in the higher decades (sixth and seventh) are slightly larger among private patients.

TABLE IX*

CASES OF RHEUMATIC HEART DISEASE GROUPED ACCORDING TO AGE, IN THE EXPERIENCE OF VARIOUS OBSERVERS

AGE GROUPS	OBSERVERS		
	FATIANOFF (BASEL)	ROMBERG (LEIPZIG)	LEUCH (ZURICH)
	%	%	%
0- 9	0.	0.15	2.0
10-19	20.8	18.8	20.3
20-29	29.8	37.2	32.0
30-39	17.9	16.2	13.0
40-49	12.4	12.7	12.5
50-59	11.0	9.1	11.2
60-69	6.0	4.3	6.6
70-79	1.5	1.0	1.6
80-89	0.5	0.1	

*Compiled from figures analyzed by Gerhardt, D., Herzklappenfehler, Wurzburg, 1913.

Unfortunately sufficient data have not yet been collected over a long enough period of time to throw any light on the question of the duration of rheumatic heart disease. It is evident that the deaths recorded in the early decades must be, for the most part, the result of rheumatic heart disease. The steepness of the slope between the fourth and fifth

TABLE X

CASES OF ORGANIC HEART DISEASE, PUBLIC AMBULATORY, PRIVATE AMBULATORY, AND WARD PATIENT GROUPS, CLASSIFIED BY SEX AND THE PRINCIPAL ETIOLOGICAL TYPES

GROUPS	ETIOLOGICAL TYPES																	
	RHEUMATIC						SYPHILITIC						ARTERIOSCLEROTIC					
	BOTH SEXES		MALES		FEMALES		BOTH SEXES		MALES		FEMALES		BOTH SEXES		MALES		FEMALES	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Total sample	449	100.	230	51.2	219	48.8	91	100.	80	88.0	11	12.0	234	100.	174	74.5	60	25.5
Public patients	408	100.	213	52.2	195	47.8	83	100.	73	88.0	10	12.0	164	100.	123	74.5	41	25.5
Private patients	41	100.	17	41.5	24	58.8	8	100.	7	87.5	1	12.5	70	100.	51	72.8	19	27.2
Ward patients	188	100.	116	16.7	72	38.3	65	100.	58	89.2	7	10.8	276	100.	216	78.3	60	21.7

decades (Fig. 1), in the mortality curve may have a significant bearing upon the question of the duration of the disease. If it were possible to break down the mortality curve showing the various types of heart diseases responsible for the deaths at the different age periods, as has been possible in our morbidity curve, interesting facts might be disclosed. Unfortunately, this is impossible under the present system of reporting deaths. In the International List of Causes of Deaths, diseases of the circulatory system are not so classified as to make possible any distinction between heart disease of infectious origin and heart disease of the degenerative type.

Sex.—In the rheumatic group we find that the proportion of the sexes is about equal (Table X). This is in agreement with a statement made by Church, that endocarditis affects the sexes equally.[8] We find a slightly greater though probably insignificant divergence between the sexes in the private patient group than in the clinic patient group. This may be attributed to the small number of cases among the private patients. In the ward patient group, on the other hand, we find almost

TABLE XI

INCIDENCE OF RHEUMATIC, SYPHILITIC, AND ARTERIOSCLEROTIC HEART DISEASE BY RACE AND NATIONALITY

ETIOLOGICAL TYPE	WHITE								COLORED	
	IRISH		ITALIAN		HEBREW		GERMAN			
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Rheumatic	72	34.6	63	58.9	72	47.2	22	30.5	16	43.2
Syphilitic	21	10.1	7	6.5	4	2.6	10	13.9	11	29.7
Arteriosclerotic	68	32.7	7	6.5	35	23.2	26	36.1	4	10.8
Other	47	22.6	30	28.1	41	27.0	14	19.5	6	16.2
Total	208	100.	107	100.	152	100.	72	100.	37	100.

twice as many males as females. Since the bed capacity in all the medical wards of the four divisions of Bellevue Hospital is twice as large for men as for women, the reason for this finding is obvious.

Race and Nationality.—Of all the cases of heart disease among the Irish, either those born in Ireland, or native-born with one or both parents born in Ireland, about one-third were rheumatic (Table XI); among the Italians, more than half; among the Germans, slightly less than one-third; among the Hebrews, slightly less than one-half; and among the colored, about two-fifths had rheumatic heart disease. When we consider the rheumatic group as a whole, we find that 16.0 per cent were among the Irish, 14.0 per cent among the Italians, 16.0 per cent among the Hebrews, 4.9 per cent among the Germans, and 3.6 per cent among the colored (Table II). It must be remembered that our immigration in more recent times has been chiefly from southern and eastern Europe. We should expect to find, therefore, a larger proportion of Italians and Hebrews among the younger of our foreign population, and consequently in the rheumatic group. With this consideration in mind,

the rather large proportion of Irish in this group may be significant, though it is evident that the data are not adequate to throw a proper light on the question of racial immunity or susceptibility to this disease. These points, however, emphasize the importance of considering the age distribution for the racial group concerned. If we had for our sample a larger number of cases, we could consider the age groupings for each of the racial groups with the view to answering questions dealing with racial immunity.

SYPHILITIC HEART DISEASE

Definition.—Among syphilitic cases we included patients, (a) who presented a definite history of syphilitic infection, and such structural changes characteristic of syphilitic heart disease as aortitis or aortic insufficiency; (b) who exhibited structural changes of the type commonly found in syphilis without a satisfactory history of syphilitic infections, but in whom the Wassermann reaction was positive; (c) who, having structural heart disease of the type usually found in syphilis, gave no past history of syphilitic infection, or positive Wassermann reaction, but who exhibited other constitutional signs of syphilis.

Age.—Syphilitic heart disease occurs primarily in the fifth and sixth decades. Although we find in our data (Fig. 5) that, consistently, for each of the three groups considered, the percentage of syphilitic cardiac disease is less than one-tenth of all heart disease, its inroad upon the most productive period of a man's life, in the ages from forty to sixty years, is a serious problem in public health. In each of the three groups, the clinic, private, and the ward patient groups, we find that the proportion of cases before and after the age of fifty years is about equal, approximately 50 per cent, the great majority of cases falling in the decade just above and that just below this age. These figures support the belief that the latent period between the syphilitic infection and the individual's awareness of resultant cardiac involvement is a long one. That structural changes must occur in these patients before they reach the age of forty, even though they may not be aware of them until failure sets in, seems evident. If this inference is correct, the data have obviously an important bearing on treatment. Here the collection of data is urgently needed.

Sex.—In the small number of cases of syphilitic heart disease available for study we find that the similarity in the three groups, clinic, private, and ward patient groups, is striking with regard to the distribution of sex (Table X). The ratio of females to males in the clinic and private patient groups is about one to seven. Among the ward patients the ratio is about one to eight. The proportion of females in this group is somewhat less than would be expected. Again, it would be necessary to increase greatly the number of cases before definite conclusions could be drawn.

Race and Nationality.—Of all cases of heart disease among the colored a little less than one-third (29.7 per cent) exhibited the syphilitic variety—about two-thirds as many as in the case of rheumatic heart disease. Among the Irish 10.1 per cent exhibited syphilitic heart disease; among the Italians 6.5 per cent; among the Germans 13.9 per cent; and among the Hebrews 2.6 per cent (Table XI). When the syphilitic

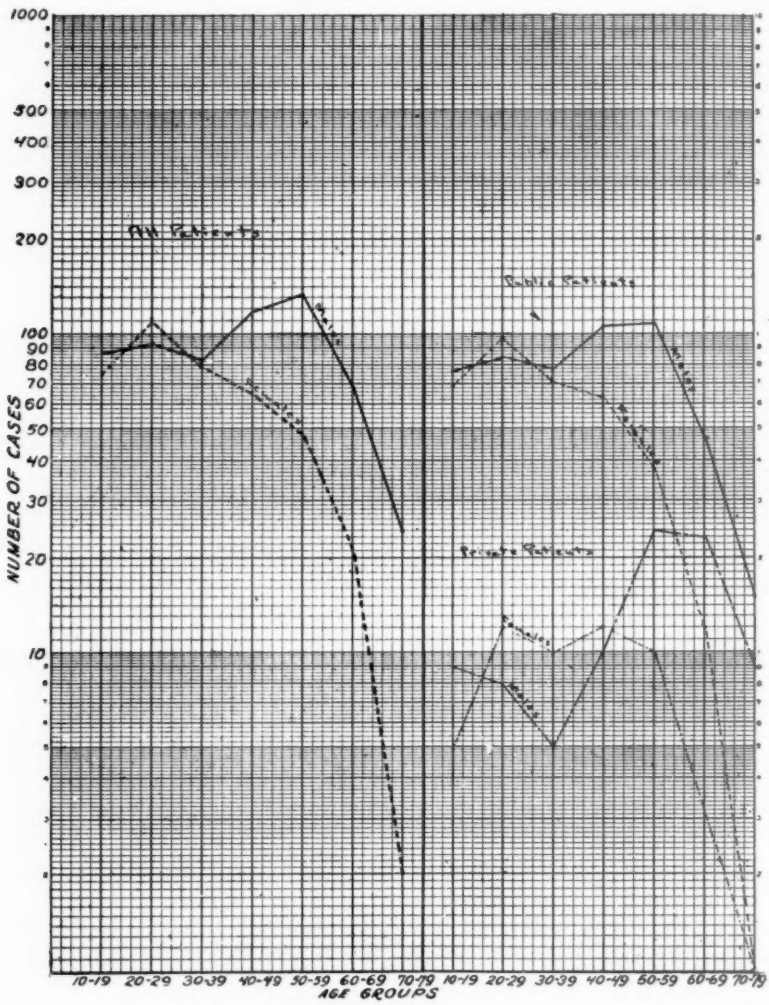

Fig. 4.—Organic heart disease by sex and age groups.

group is considered, the proportions are 23.1 per cent Irish, 11.0 per cent German, 7.7 per cent Italian, 4.4 per cent Hebrew, and 12.1 per cent colored (Table II). Here again the numbers are so small that the percentages are unreliable. The rather large proportion of Irish and colored and the small proportion of Hebrews might be significant data if they were corroborated by a greater number of cases.

ARTERIOSCLEROTIC HEART DISEASE

Definition.—In the arteriosclerotic group are included patients who presented signs of cardiac defect commonly associated with arteriosclerosis in the absence of syphilis, nephritis with nitrogen retention, gout, and diabetes. When arteriosclerosis was present coincident with any of these diseases we considered the cases as heart disease, secondary to syphilis, nephritis, diabetes, or gout.

Age.—That this form of heart disease concerns itself chiefly with the sixth, seventh, and eighth decades, occurring rarely before fifty years of age is substantiated by our data (Figs. 4 and 5). An attempt was made in the early part of this paper to account for the relatively small number of cases after the seventh decade, and in the sixth decade in the clinic patient group. The smaller proportion, under fifty years, in the private than in the clinic group, and the smaller percentage of cases in the sixth than in the seventh decade among the private patients, as contrasted with the clinic patients, may bear evidence on the possibility of postponement of the disease by early treatment and corrected habits of living.

Sex.—In this group we find again consistency in the proportion of males to females for both the clinic and private patient groups (Table X). Why there are apparently so many more men than women suffering from this type of heart disease is not to be accounted for. The larger bed capacity for men than women might account in part for the divergence in the ward patient group. It might also be reasonably true that women in the older age groups refuse to go to the clinic for treatment even more persistently than men. But why the smaller percentage of women than men is found also in the private patient group is hard to understand, unless the desire or necessity to keep fit for economic reasons, on the part of men, plays a part here. Analysis of the death rate for the sexes in these age periods would lead one to expect to find that the disease affects the sexes equally.

Race and Nationality.—Of the cases of heart disease among the Irish about one-third were arteriosclerotic, among the Italians only 6.5 per cent, among the Hebrews about one-fourth, of the Germans slightly more than one-third, and among the colored 10.8 per cent (Table XI). Of the total group of arteriosclerotic cases the largest proportion, 29.1 per cent was Irish, 15.0 per cent Hebrew, 11.1 per cent German, 3.0 per cent Italian, and 1.7 per cent colored (Table II). Since arteriosclerosis is a disease that affects individuals usually after the age of forty, its more frequent occurrence among the Irish and Germans, who constitute chiefly the older age groups in our foreign population, than among the Italians, is what we should expect to find. On the other hand, the proportion of Hebrews in this group is relatively larger than we should expect. It is possible that the immunity to tuberculosis and other dis-

cases that seems prevalent among the Hebrews spares them for a higher age at which the degenerative diseases claim their victims.

UNKNOWN ETIOLOGY

In the group in which the etiology is given as "unknown" are included patients who had signs of structural cardiac change or definite signs of diminution of cardiac reserve in which no definite etiology could be determined. As many of these cases presented lesions typical of the

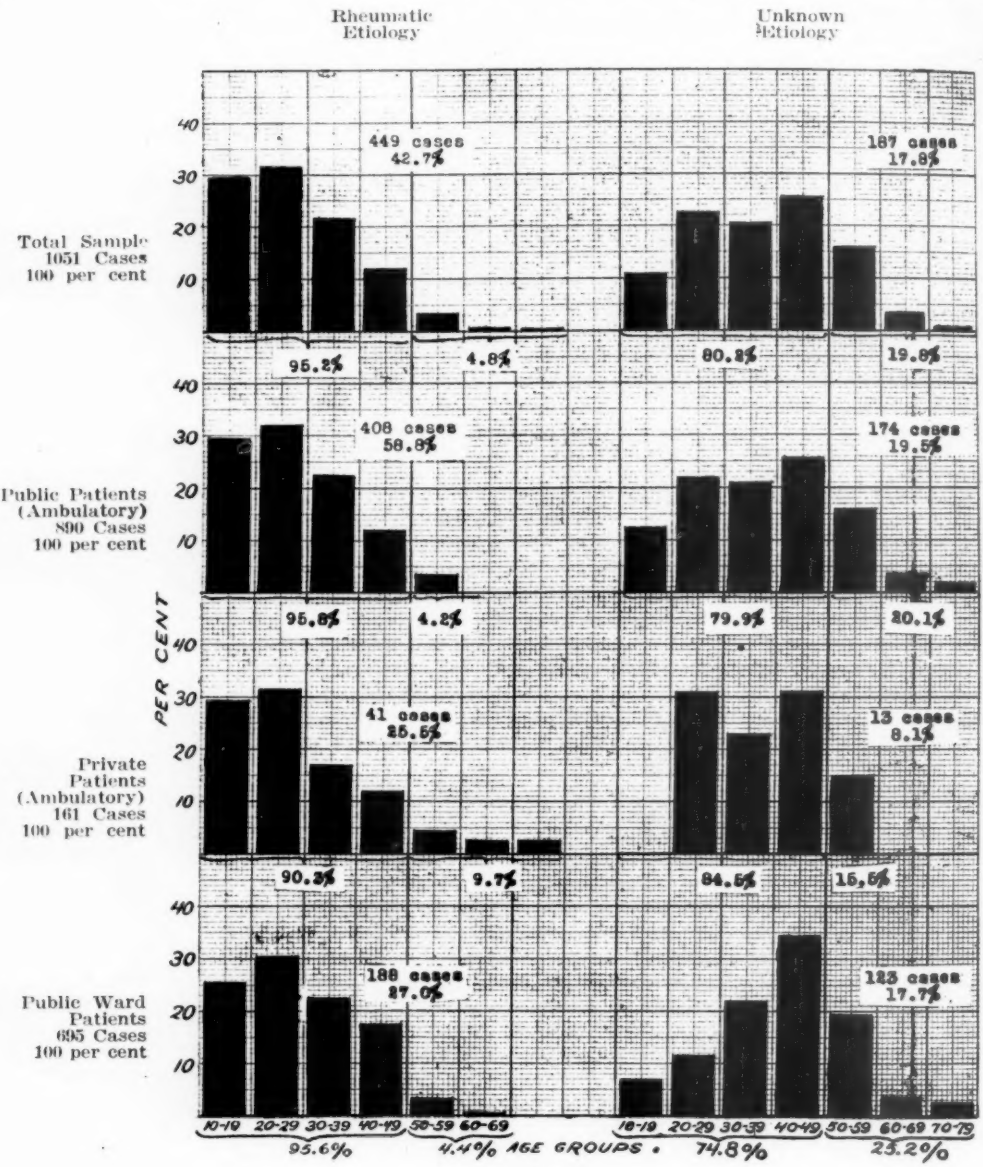

Fig. 5.

rheumatic form of heart disease an attempt was made to reclassify them as rheumatic, syphilitic, etc., on the basis of the typical lesion, regardless of any etiological history. It was found that two-thirds, 63.9 per cent, of these cases presented lesions typical of rheumatic heart disease, 6.7 per cent presented lesions typical of syphilitic heart disease, and the remaining 29.4 per cent presented lesions not typical of any definite etiological group. The probability that a large proportion of these cases

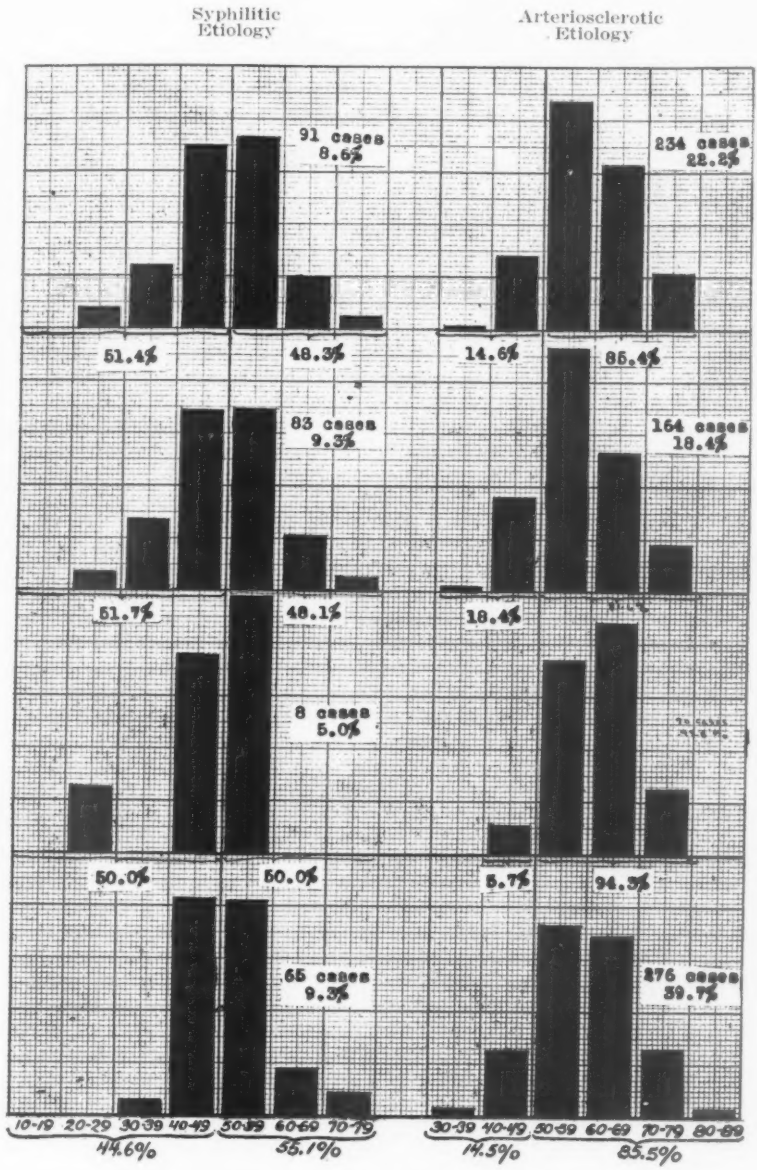

Fig. 5.

is rheumatic may further be borne out by the fact that between 75 and 90 per cent of the cases occurred before the age of fifty. It is believed that the absence of a definite rheumatic history in such cases may be due to the fact that the heart muscle or valves were affected rather than the joints. Subsequent rheumatic manifestations in the joints are not uncommon in cases of organic heart disease in which there is a lesion of the rheumatic type and in which there is an "unknown" etiology.

OTHER ETIOLOGICAL FACTORS

Etiological factors other than those discussed up to this point comprised 8.6 per cent of the total sample (Table VI). Of these, disease of the thyroid gland was a factor in seventeen instances, or 1.1 per cent of the whole number of cases. Since we have been particularly watchful for this ailment as a factor in heart disease, we are interested in finding this percentage so low. We found congenital malformation in seven instances. We found fifteen cases of hypertensive heart disease, an etiological diagnosis made when there was hypertension with no sign of arteriosclerosis or nephritis. Under chronic nephritis we include only such cases as show definite signs of nitrogen retention or albuminuric retinitis, in addition to arteriosclerosis or hypertension. Under this heading we had seven cases. In seven cases the etiology was an infection of bacterial origin; in five the etiological factor was diabetes; in five, chronic bronchitis or emphysema or asthma; in four, arthritis or gout; and in one case trauma. The last named was a definite case of a stab wound of the heart. In the remaining twenty-three cases no etiological factor was recorded.

SUMMARY

In the foregoing analysis of 1001 cases of organic heart disease among adults, we found that:

1. There was a close resemblance among the histograms representing the three prominent types of heart disease for the clinic patient, private patient, and ward patient groups (Fig. 4).

2. About one-fourth of the cases presented rheumatic heart disease, about two-fifths arteriosclerotic, about one-tenth syphilitic, and about one-tenth heart disease of unknown origin; other factors, such as scarlet fever, hyperthyroidism, nephritis, etc., together, comprised less than one-tenth of the total sample.

3. A comparison with the mortality curve led to the belief that the private and ward groups were more representative of organic heart disease, so far as age and etiology are concerned.

4. Rheumatic heart disease was rare after fifty years of age; from 90 to 95 per cent of the cases of rheumatic heart disease occurred before the age of fifty years, more than half of which occurred before the age

of thirty. About 50 per cent of the syphilitic cases occurred before the age of fifty, and 50 per cent after this age; the disease appeared to be rare before the age of forty and after the age of sixty. From 80 to 95 per cent of the cases of arteriosclerotic heart disease occurred after fifty years of age. Two-thirds of the cases of unknown etiology presented lesions typical of rheumatic heart disease, and occurred before the age of fifty.

5. In about three-fourths of the cases of rheumatic heart disease rheumatic fever, either alone or in combination with other infections, was an etiological factor; tonsillitis, in one-fourth of the cases; chorea, in a little more than one-tenth of the cases, and growing or joint pains, in about one-twentieth of the cases. With the exception of chorea, which occurred twice as often among females as males, the relative frequencies of these infections was about equal for the sexes.

6. Rheumatic heart disease seemed to be as common among males as among females. In syphilitic heart disease the ratio of males to females was about seven or eight to one; arteriosclerotic heart disease appeared to be much more common among males than among females. The reason for this is inexplicable since the mortality from heart disease is about equal for the sexes in the higher age groups.

7. Foreign-born whites made up almost half of the total sample. Little could be learned about the predominance of race or nationality in any of the types of heart disease, both on account of the small number of cases, and because of the fact that age and etiology seem to be so closely related, and that the older immigrants, the Irish and the Germans, constitute the older age groups, and the newer immigrants, the Italians and the Hebrews, the younger age groups. With these points in mind, the rather large proportion of Irish found in the rheumatic group, the rather large proportion of Irish and colored, and the small proportion of Hebrews in the syphilitic group, and the relatively large proportion of Hebrews in the arteriosclerotic group suggest that a detailed study, comprising a larger number of cases, along this line is desirable.

While it must be strongly emphasized that no conclusive deductions can be drawn from the foregoing analysis on account of the small number of cases, this study should, nevertheless, focus attention upon the following points:

1. The available mortality statistics for organic heart disease are inadequate in any attempt to study the age incidence and duration of the disease, because they are based on deaths recorded in accordance with the International List of Causes of Death which is not so classified as to make it possible to distinguish between the infectious and degenerative varieties of the disease.

2. By introducing into clinics a uniform system of records and organizing clinics in such a way as to facilitate the collection of facts for sta-

tistical purposes, reliable and important data concerning heart disease may be made available.

3. It is only when heart disease is treated in special cardiac clinics or wards or by physicians who are specialists in heart disease, and when these agree upon uniform methods of seeking, describing, and recording the facts as they present themselves in individual cardiac cases, that sufficient data can be collected and any progress be made in understanding the problems with which this study deals.

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A CLINICAL STUDY OF DIGITALIS BIGEMINY*

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THE two commonest and earliest signs of overdigitalization in man are vomiting and premature contractions of ventricular origin These have long been considered as minor toxic signs and as indication for withdrawal of the drug. They have served in a sense as a protective mechanism against more serious overdosage. It has not been difficult to assess their value from this standpoint when, in a patient with auricular fibrillation, a rapid ventricular rate has been reduced to 60 or 50 per minute, the signs of heart failure have disappeared, and, when with the continuation of the drug, nausea and vomiting or premature contractions have set in. In such a patient they are clearly evidence of overdosage. However, in the treatment of large numbers of cardiac patients with digitalis over long periods of time, one can hardly escape the conclusion that the subject of vomiting and premature contractions occurring in some of these patients is not quite so simple a matter as is implied in the statement that they are merely evidences of overdosage. Thus, from time to time, patients are seen in whom these signs seem to be not so much a protection against overdigitalization as a hinderance to effective digitalization. The differences should obtain in the conditions attending the onset of digitalis vomiting or premature contractions does not appear remarkable when one considers the possibilities for variation in the sensitiveness of the vomiting mechanism concerned with digitalis emesis or in the properties of the heart in disease that render it more or less susceptible to the production of premature contractions. These differences have not been adequately investigated. Vomiting from digitalis has received considerable attention in animal experimentation. There has not been much clinical study of the subject.

There are even fewer contributions in the literature to the problem of coupled rhythm resulting from digitalis. From time to time isolated cases have been reported. However, in 1916, Edens and Huber[1] published an analysis of 29 cases of digitalis bigeminy and, since that is the only study of a considerable group of patients we were able to find, we shall have occasion to refer frequently to the salient points of that work.

SCOPE AND METHOD OF INVESTIGATION

During the past three years, 855 patients with organic heart disease were admitted to the Third Medical Division of Bellevue Hospital. Of

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these, 569 patients received digitalis. Eight per cent of the latter, or 45 patients, developed digitalis bigeminy. These form the basis of the present study.

The coupled rhythm in these patients arose in the course of the routine management of their heart failure. On the Third Medical Division of Bellevue, it is the routine procedure to delay digitalis medication, except in urgent cases, for one week after admission in order to ascertain the effect of rest, limited fluid intake, and diet. The patients are then digitalized with the tincture of digitalis—0.1 cat unit per pound of body weight—in four doses at six-hour intervals as suggested by Eggleston.[2] The next day medication is omitted and on the day following a daily maintenance dose is instituted, the size being arbitrarily selected and increased or diminished according to the patient's needs.

All patients with organic heart disease under digitalis treatment in the wards of this service and in the Adult Cardiac Clinic of the Out-Patient Department were carefully observed for the inception of the toxic rhythm. It arose after the initial digitalization in 8 patients. In the remaining 37 patients, it was first seen after daily maintenance doses for varying periods of time. Patients developing this rhythm in the cardiac clinic were admitted to the ward where daily records were made of the ventricular rate, pulse deficit, the symptoms and the persistence of the bigeminy. Electrocardiograms were taken at frequent intervals. On discharge from the ward, these patients were again referred to the clinic for further observation.

It was not difficult to establish the causal relation of the drug to the bigeminal rhythm. In the first place, persistent spontaneous bigeminy, due to auricular or ventricular premature contractions, is very uncommon. It occurred in only 7 patients or 0.8 per cent of the total group of cardiac patients before the administration of digitalis. These are not included in the present study. In the remaining patients the bigeminal rhythm was not present before the drug was given, it would disappear after varying periods following the withdrawal of the drug, and it could be made to reappear when the administration of the drug was resumed.

It is our purpose in the present report to present an analysis of these 45 cases and to bring evidence to bear as far as possible upon certain moot questions pertaining to digitalis bigeminy.

ANALYSIS

In all the 45 patients, the bigeminal rhythm was due to the occurrence of premature contractions arising after each normal beat in either the right or the left ventricle. The shape of the aberrant complex was constant in any single electrocardiogram in the majority of patients, but in a few they were variable in shape and size. In only one case,

which will be discussed later, did there seem to be any relation between the clinical condition or the prognosis and the irregularity in shape of the ventricular complexes.

TABLE I

SHOWING THE ABSOLUTE AND RELATIVE DISTRIBUTION OF 45 PATIENTS WITH DIGITALIS BIGEMINY IN TEN YEAR GROUPS, COMPARED WITH A CONTROL GROUP OF 855 CARDIAC PATIENTS

	Control group of 855 cardiac patients		*Forty-five patients with digitalis bigeminy*	
AGE GROUPING	ACTUAL INCIDENCE	PERCENTAGE INCIDENCE	ACTUAL INCIDENCE	PERCENTAGE INCIDENCE
10-19	77	9	6	13
20-29	98	11.5	3	7
30-39	103	12	13	29
40-49	188	22	6	13
50-59	214	25	12	27
60-69	129	15	5	11
70-79	46	5.5	–	–
	855	100	45	100

Table I shows the age distribution of the 45 patients with digitalis bigeminy. While it occurred in patients from twelve to sixty-four years of age, the table shows a relatively greater incidence of the toxic rhythm before the age of forty. This is quite at variance with the findings of Edens and Huber, who stated that only 20 per cent of their patients were below the age of forty.

Of the 45 patients, 26 were males and 19 females. This is about the proportion of males to females in the entire group of cardiac patients.

TABLE II

COMPARING THE ABSOLUTE AND RELATIVE INCIDENCE OF THE ETIOLOGICAL TYPES OF HEART DISEASE IN WHICH BIGEMINY OCCURRED WITH THEIR INCIDENCE IN A CONTROL GROUP OF 855 PATIENTS

	Control group of 855 cardiac patients		*Forty-five patients with digitalis bigeminy*	
ETIOLOGICAL TYPE	ACTUAL INCIDENCE	PERCENTAGE INCIDENCE	ACTUAL INCIDENCE	PERCENTAGE INCIDENCE
Arteriosclerotic	299	35	8	18
Rheumatic	205	24	16	36
Unknown	180	21	15	33
Syphilitic	77	9	4	9
Other	94	11	2	4
	855	100	45	100

Table II is arranged to compare the absolute and relative incidence of the etiological types of heart disease in which bigeminy occurred, with their incidence in the total group of cardiac patients. In a study

soon to be published, Wyckoff and Lingg[3] define these etiological types and show that the unknown group is largely made up of rheumatic heart disease. These cases are not included in the rheumatic group, because, although the structural lesion is characteristic of rheumatic heart disease and the age grouping is similar, there is no definite history of polyarthritis, chorea, growing pains or repeated attacks of tonsillitis. On study of this table, it is at once apparent that there is a diminution of both the absolute and relative incidence of bigeminy in the arteriosclerotic group, the incidence in the rheumatic group being proportionally increased. It is also seen that digitalis bigeminy may occur in any etiological type of heart disease. In our group of cases, it was found with greater frequency in the rheumatic than in any other type.

Structural Lesions.—All 45 patients showed cardiac enlargement. This is of interest in view of the emphasis by Edens and Huber upon the statement that digitalis bigeminy occurred only in insufficient and enlarged hearts. In the great majority of these cases the hearts were enormous. The diagnosis of adhesive pericarditis and tricuspid stenosis were only included when confirmed at autopsy. The diagnosis of aneurysm and aortic dilatation was confirmed by x-ray. The same was true for the diagnosis of enlarged heart. The diagnosis of mitral stenosis and insufficiency and aortic insufficiency was determined by the classical subjective and objective findings. It is seen from Table III that 34 patients had some valvular lesion; the mitral valve being most frequently affected, alone or in combination with other valves in 25 patients, the aortic valve involved in 12, and the tricuspid in 3 patients. In 3 patients, there was adhesive pericarditis obliterating the pericardial sac. It is evident that in the group of patients with digitalis bigeminy all the common structural forms of heart disease are represented.

In 68 per cent of the 855 patients, the basic rhythm was a regular sinus rhythm that may or may not have been interrupted by occasional premature contractions. The basic rhythm in 28 per cent was auricular fibrillation. The incidence of sinus rhythm and auricular fibrillation in the 45 patients with digitalis bigeminy was reversed. In 35 cases or 78 per cent, there was auricular fibrillation; in 10 cases or 22 per cent, there was a regular sinus rhythm. Of the patients with a regular sinus rhythm receiving digitalis, 2.8 per cent developed bigeminy. Of the patients with auricular fibrillation receiving digitalis, 17 per cent developed bigeminy. The toxic rhythm occurred therefore 6 times as often in patients with auricular fibrillation as in those with a regular sinus rhythm. This is not the impression one gains from the report of Edens and Huber, whose 29 patients were about equally divided between those with auricular fibrillation and those with a regular sinus rhythm, although they did not relate their data to the total number

TABLE III

SHOWING DISTRIBUTION OF STRUCTURAL LESIONS IN 45 PATIENTS WITH DIGITALIS BIGEMINY

	RHEUMATIC	UNKNOWN	ARTERIO-SCLEROTIC	SYPHILITIC	OTHER
Number of cases	16	15	8	4	2
Enlarged heart	16	15	8	4	2
Aortitis with dilatation					
Mitral insufficiency alone		1			
Mitral stenosis and insufficiency	12	5			
Aortic stenosis and aortic insufficiency					
Mitral stenosis and insufficiency, and aortic stenosis and insufficiency	1				
Mitral stenosis and insufficiency and tricuspid stenosis and insufficiency					
Aortic insufficiency alone		1		3	
Adhesive pericarditis with mitral insufficiency and tricuspid stenosis and insufficiency		1			
Adhesive pericarditis with mitral stenosis and mitral insufficiency	1				
Adhesive pericarditis with mitral stenosis, mitral insufficiency, aortic stenosis, aortic insufficiency	1				
Mitral insufficiency, aortic stenosis and insufficiency	1				
Mitral stenosis and insufficiency and tricuspid stenosis and insufficiency		1		1	
Aneurysm of aorta with aortic insufficiency				2	
Aortitis with aortic insufficiency		3			

of cases seen. Of the 10 patients in our group with a regular sinus rhythm, only 2 retained that rhythm after the administration of the digitalis. The remaining 8 began to fibrillate either before, simultaneously with, or following, the occurrence of the coupled rhythm.

RELATION OF PREMATURE CONTRACTIONS TO COUPLED RHYTHM

In some patients, digitalis often induces ventricular premature contractions which increase in number as the drug is continued until a definite coupled rhythm is produced. When the drug is discontinued, the coupled rhythm does not disappear at once, but the premature contractions become less frequent and persistent, occurring in small groups until they gradually disappear entirely. From this behavior alone, it would seem that the premature contraction produced by digitalis was simply a lesser degree of the same type of effect which results in a coupled rhythm. Certain questions have arisen. Does the occurrence of spontaneous premature contractions signify an increased susceptibility to digitalis bigeminy? Does the occurrence of premature contractions as a result of digitalis imply that that heart is, or ever will

be, particularly liable to digitalis coupling? An analysis was made of a group of 86 patients with auricular fibrillation receiving digitalis during a period of three years, under careful observation in the out-patient department. Of the 60 patients living, three-fourths showed premature ventricular contractions. Of the 26 patients deceased, over four-fifths showed premature contractions. The number showing premature contractions at some time probably approaches more nearly 100 per cent of patients with auricular fibrillation than these figures indicate, considering the possibility for missing occasional premature contractions when only short strips of electrocardiogram are taken. The fact that nearly all patients with auricular fibrillation receiving digitalis at some time show premature ventricular contractions and only about 17 per cent of them develop digitalis bigeminy, points to another factor responsible for the bigeminy that is not indicated by the occurrence of premature contractions either spontaneously or as a result of digitalis as will be shown.

RELATION OF BIGEMINY TO THE LENGTH OF TIME UNDER MEDICATION

A certain number of patients receiving digitalis over a long period of time seem to become particularly susceptible to its toxic action. This has given rise to the thought that the prolonged use of the drug produces a sensitization, with the result that a coupled rhythm occurs with such small doses as to make it impossible to digitalize effectively without this toxic rhythm. There is considerable individual variation in the length of time under digitalis medication and in the total quantity of the drug taken before the coupled rhythm appears. At one extreme, we have a patient with a functionally poor heart that fails to show any improvement from rest in bed and digitalis, showing bigeminy only after nearly 6000 grains of digitalis leaf had been consumed over a period of about three and one-half years. At the other extreme, there is a patient with a functionally good heart responding readily and satisfactorily to treatment, but showing a digitalis bigeminy after a total of only 40 grains of the powdered leaf over a period of two weeks. The average of the total length of time under digitalis medication for 34 patients of this group is twenty-one months, as against thirty-eight months for a control group of 34 patients with auricular fibrillation not showing this rhythm under similar treatment. These data, therefore, lend no support to the view that the length of time under digitalis medication determines increased susceptibility to digitalis bigeminy.

PERSISTENCE OF DIGITALIS COUPLING

Table IV shows the duration of digitalis coupling after withdrawal of the drug. The average for the 22 patients in whom it was determined is about ten days. As is seen in the table, the duration varies considerably with different patients as well as in the same patient under

different conditions, the bigeminal rhythm lasting from three days to thirty-four days in different patients of this group and from seven days, at one time, to as long as twenty-eight days at a subsequent time in the same patient. In only three cases was a second determination made of the duration of the coupled rhythm. It is of interest to note that with increasing myocardial insufficiency some patients not only become more sensitive to the production of the bigeminal rhythm, but the heart tends to recover more slowly from the effects of the drug.

TABLE IV

SHOWING THE PERSISTENCE OF DIGITALIS BIGEMINY AFTER WITHDRAWAL OF THE DRUG

	Duration in days	
PATIENT	FIRST DETERMINATION	SECOND DETERMINATION
1	7	8
8	10	
9	10	
11	6	
12	34	
13	7	28
14	4	
15	6	
16	8	
18	5	
19	4	10
21	12	
22	10	
24	12	
28	21	
29	10	
31	11	
32	5	
37	4	
42	3	
43	14	
45	8	

FUNCTIONAL CLASSIFICATION AND PROGNOSIS

Edens and Huber said that, after two years, 80 per cent of their 29 patients with digitalis bigeminy had died. Of the 41 patients in our series whose present status is known, collected in a period of three years, only 51 per cent have died. Willius[4] reported that, of 500 patients with auricular fibrillation collected over a period of four and one-half years, 41 per cent had died. The high mortality for our series of patients with digitalis bigeminy is therefore not so striking in view of the fact that 43 of the 45 patients had auricular fibrillation.

These general averages convey a very imperfect idea and create perhaps an erroneous impression of the type of patients in whom digitalis may induce a bigeminal rhythm. We thought it would be profitable therefore to record some typical cases in greater detail.

CASE 1.—Patient, female, twenty-nine years of age, was admitted to the hospital with a history of heart failure of three months' duration. The diagnosis was heart disease of unknown origin, mitral stenosis and insufficiency, enlarged heart and auricular fibrillation. She was fully digitalized in the hospital three different times,—in each case with 0.10 cat unit, per pound of body weight, of the tincture in the course of twenty-four hours. As a result, all symptoms of failure disappeared and the ventricular rate was reduced to 70 per minute, with no pulse deficit. After discharge from the hospital, she was given three grains daily of the powdered leaf for two weeks, which maintained the above clinical condition. The dose was increased to four grains of the leaf daily and after four weeks, although the symptoms remained unchanged, the ventricular rate was reduced to 58 per minute and coupled rhythm appeared. Since that time the patient has been doing regular housework with practically no symptoms of failure and no bigeminy on smaller doses of digitalis.

Summary.—Digitalis bigeminy in a patient with good cardiac reserve who responded readily and satisfactorily to treatment. Maximum improvement obtainable occurred before the bigeminy appeared and with doses smaller than those necessary to produce coupling. Patient received digitalis, in all, over a period of two and one-half months.

CASE 2.—Patient, male, thirty-four years of age, was under our observation in the out-patient department. History of heart failure of four years' duration. A diagnosis was made of heart disease of unknown origin, enlarged heart, mitral stenosis and insufficiency and auricular fibrillation. During the four years, he received more or less continuously a daily dose of digitalis, ranging between 2 and 4 grains of the powdered leaf, and continued at his work as a chair caner in comparative comfort. When his symptoms of failure grew worse from overwork, increased rest and digitalis resulted in improvement and the ventricular rate was often decreased to as low as 48 per minute. On some occasions, the patient felt best at this low rate; at other times, nausea was induced. After a time, however, the symptoms of failure began to grow progressively worse so that the patient was compelled to give up his work. Now, an increase in the dose of digitalis not only failed to cause improvement in the symptoms, but gave rise to coupled rhythm. At first, it was only with the larger doses that this rhythm was produced. The symptoms of failure, however, became progressively worse and the coupled rhythm became more and more persistent, being now evoked even by the smaller doses. Nine months after the appearance of the coupled rhythm, corresponding approximately to the period in which the symptoms of failure began to resist treatment, the patient died in congestive heart failure.

Summary.—Digitalis bigeminy in a patient with poor cardiac reserve, who failed to improve under treatment and in whom susceptibility to the toxic rhythm developed hand in hand with loss of contractile power of the heart; received digitalis almost continuously over a period of four years.

CASE 3.—Patient, male, forty-three years old, was under our care in the cardiac clinic with a history of heart failure of two years' duration. A diagnosis was made of heart disease of unknown origin, enlarged heart, and auricular fibrillation. In July, 1923, he was admitted with symptoms of heart failure, rapid ventricular rate and pulse deficit. On three grains of powdered digitalis leaf daily for one month and four grains daily for four months the symptoms of failure disappeared and the ventricular rate was reduced and maintained at about 70 per minute without

a pulse deficit. In April, 1924, about nine months later, having had no digitalis for several months, the patient returned to the clinic with symptoms of failure similar to those of his first admission. This time, 4 grains daily for 3 weeks, of the same preparation employed the first time, removed all symptoms of failure but induced a coupled rhythm with a ventricular rate at 56 per minute. Since then the patient has worked for 17 months as a porter with no symptoms of failure and a ventricular rate of 80 to 85 per minute with no pulse deficit or bigeminy, receiving no digitalis.

Summary.—Susceptibility to bigeminy developing in a patient with good cardiac reserve without any apparent change in the functional capacity of the heart. Received digitalis with several intermissions over a period of two years.

The entire series of patients with digitalis bigeminy falls into several more or less distinct groups as seen in Table V. It might be well to recall at this point, that in the large majority of patients with auricular fibrillation, digitalis cannot induce a bigeminal rhythm in doses as large as may be given with reasonable safety, these being considerably in excess of therapeutic doses. We have carried digitalization in patients until the ventricular rate was reduced to 30 per minute, occasional premature contractions induced, and persistent nausea and vomiting. For all practical purposes, these patients may be considered as not susceptible. From the functional standpoint, these represent all types of patients, from those with clinically good hearts, who respond readily to treatment and can be maintained at their usual work with few or no symptoms of failure, to those with functionally poor hearts, with bundle-branch block, who fail to improve under treatment and who are practically incapacitated by their heart failure. All patients who present digitalis bigeminy regardless of the dose of the drug are to be considered as possessing especial susceptibility. From the standpoint of the functional capacity of the heart, patients susceptible to digitalis bigeminy fall, broadly speaking, into two classes. First (Groups I and II of Table V), are those in whom susceptibility to the toxic rhythm runs hand in hand with increasing myocardial failure. This class is represented by 21 of the 45 patients of our series, 18 of whom died in from two days to nine months after their bigeminy was first recorded. Edens and Huber said that the poor prognosis in patients with digitalis bigeminy depends partly upon the fact that the bigeminy interferes with effective digitalization, implying that if the bigeminy could be prevented, the prognosis would be better. From the behavior of this group of patients, one can hardly gain that impression. These patients have extreme heart failure which is growing progressively worse and they have begun to resist all forms of treatment, showing little or no improvement from rest in bed or digitalis in any doses. They behave like any cardiac patient without digitalis bigeminy who has ceased to respond to treatment. They are patients with heart disease in the terminal stage.

TABLE V

CLASSIFYING THIRTY-NINE PATIENTS WITH DIGITALIS BIGEMINY INTO FOUR GROUPS SHOWING LENGTH OF TIME SINCE BIGEMINY WAS FIRST NOTED AND PRESENT STATUS OF PATIENT

NO.	DAYS OBSERVED AFTER BIGEMINY FIRST NOTED	PRESENT STATUS	
1	90	dead	
2	60	dead	
3	35	dead	GROUP I.
4	30	dead	Consisting of patients in extreme heart failure
5	30	dead	unimproved by rest in bed or digitalis in any
6	9	dead	dosage. All died in from two days to three
7	9	dead	months after the bigeminy was first recorded.
8	6	dead	
9	3	dead	
10	2	dead	
1	700	dead	
2	270	dead	GROUP II.
3	180	dead	Consisting of patients who showed slight
4	150	dead	functional improvement under digitalis medica-
5	60	dead	tion. All but three died in from two weeks to
6	60	dead	two years after bigeminy was first noted.
7	21	dead	Though all patients of this group were able,
8	14	dead	for sometime, to be about, they were almost
9	350	serious	totally incapacitated.
10	300	serious	
11	210	serious	
1	910	dead	
2	700	dead	
3	330	serious	
4	700	good	
5	410	good	GROUP III.
6	330	good	Consisting of patients showing marked clinical
7	300	good	improvement under digitalis medication. All
8	290	good	patients of which we know are alive, except
9	225	good	two, one seriously ill, and the remaining eight
10	210	good	are in good condition.
11	210	good	
12	195	good	
+13	210		
+14	90		
+15	28		
1	1225	good	GROUP IV.
2	840	good	Consisting of patients who developed increased
3	525	good	susceptibility to digitalis bigeminy during
			active carditis (rheumatic), disappearing on
			subsidence of activity. All three patients are
			well after periods of one and one-half to three
			and one-half years after the first appearance
			of bigeminy.

+These patients were lost track of after having been under observation the number of days indicated.

In the second class (Group III of Table V), are those who present relatively good myocardial function, considering the fact that, having auricular fibrillation, they are all patients with serious heart disease. Since these patients develop susceptibility to digitalis bigeminy without

any apparent change in the functional capacity of the heart, the toxic rhythm occurring in them presents considerable interest from the prognostic standpoint. How long do these patients live after the development of a bigeminal rhythm from digitalis? Does the bigeminy indicate grave prognosis independent of the functional capacity of the heart?

Our patients belonging to this class have not been followed long enough to answer these questions adequately. Of the 12 patients of this group only 2 have died, in two years and two and one-half years respectively after digitalis bigeminy was first recorded. The longest period since the onset of coupling among those living is only two years.

The three patients who developed increased susceptibility to digitalis bigeminy only during an acute infection are all living, one and one-half years, two years and four months, and three and one-half years, respectively, after the first record of bigeminy.

From analogy with related conditions, there is no evidence to justify the conclusion that digitalis bigeminy *per se* indicates grave prognosis beyond that obtained from the functional capacity of the heart. Premature contractions occur in patients with otherwise normal hearts. In diseased hearts Willius has shown that the mortality for patients with auricular fibrillation complicated by premature contractions is practically the same as that for patients with auricular fibrillation without premature contractions. Similarly, we have seen a bigeminal rhythm appear spontaneously in a patient sixty-one years of age with a badly damaged arteriosclerotic heart three days before death. On the other hand, we have a patient thirty-one years of age showing a spontaneous coupled rhythm, who two and one-half years after an attack of heart failure has been doing hard work as a truck driver, with no signs of heart failure and receiving no digitalis.

The relation of the functional capacity of the heart to the degree of susceptibility to digitalis bigeminy may be such that clinical improvement appears and can be maintained only with those doses of digitalis that call forth a coupled rhythm. On the other hand, the heart may be so resistant to digitalis bigeminy that the maximum obtainable functional improvement occurs, and can be maintained, with doses of the drug much smaller than those necessary to induce in that patient a coupled rhythm.

In the treatment of heart failure those patients who show maximum obtainable improvement before the onset of coupling present little difficulty. The margin of safety is comparatively wide and, with competent use of the drug, the therapeutic effect can be obtained in the absence of a coupled rhythm. We wish to call attention, however, to a possible danger in the treatment of that group in whom functional improvement occurs simultaneously with the onset of the toxic rhythm. This was suggested by the behavior of one of our patients.

Patient, female, aged thirty-one years, had a history of heart failure of three and one-half years' duration. The diagnosis was rheumatic heart disease, mitral stenosis and insufficiency, and enlarged heart. After treatment by her physician with digitalis for about 5 weeks with little improvement, she was admitted to the hospital in marked heart failure. Following six days of rest in bed, the symptoms remained practically the same and the ventricular rate was 150, with a pulse deficit of 30. She received 19 c.c. of the tincture of digitalis in 24 hours, the ventricular rate being reduced to 70 per minute, with no deficit. Two grains of the powdered digitalis leaf daily for three days failed to maintain this rate. The dose was increased to three grains daily. After the fifth three-grain dose, coupling set in, with the ventricular rate at 80 per minute. During the period of coupling there was considerable improvement in the clinical condition, many of the symptoms of failure disappeared and the patient was walking about comfortably on the ward. Four more daily doses of three grains each were given and on the fifth day, the patient died suddenly.

Electrocardiograms taken at frequent intervals proved to be of especial interest. Before the digitalis, the electrocardiogram showed auricular fibrillation with a rate of 140 and an occasional premature contraction. When the coupled rhythm set in, the rate was 80, with premature contractions of uniform shape originating in the right ventricle. As the drug was continued, the ventricular complexes of the premature beats became more and more varied in shape, the dominant premature beat changing to left ventricular origin. The greatest irregularity was seen about eight hours before death when the electrocardiogram showed small groups of three to four aberrant beats in succession, resembling closely the prefibrillary state described by Levy and Lewis.[5]

Obviously, one cannot be certain of the exact cause of death in this patient, but the progressive changes in the electrocardiogram indicate that digitalis had at least produced dangerous alterations in the properties of the heart.

It has been stated that patients in whom digitalis has produced a bigeminal rhythm are particularly prone to die suddenly. We do not have exact data of the relative incidence of sudden death in patients with heart disease not susceptible to digitalis bigeminy for comparison. It is well to state, however, as a matter of record, that of 21 of our patients whose mode of death was definitely known, it occurred by progressive heart failure in sixteen. Five patients died suddenly. In one of the latter cases it is not known whether digitalis was being taken at the time of death. Two patients were taking three grains daily of the powdered digitalis leaf. The remaining two patients had been without digitalis for fourteen and thirty days, respectively, prior to their sudden death.

ACTION OF ATROPINE ON DIGITALIS BIGEMINY

Edens and Huber said that they had observed no effect of atropine upon a well-developed bigeminy. They did not record the doses of the drug used. Cushny, et al,[6] gave $\frac{1}{50}$ grain of atropine to a patient with

auricular fibrillation and digitalis bigeminy, with no effect upon the coupled rhythm. More recently, T. S. Hart[7] has stated that digitalis coupling can be abolished by $\frac{1}{75}$ grain atropine. We tested the effect of atropine upon well-developed digitalis bigeminy in five patients. Two or three one-minute electrocardiograms were taken as controls at about ten-minute intervals before the administration of the drug. The patient then received 4 milligrams of atropine sulphate subcutaneously. At ten-minute intervals for the first hour and at longer intervals subsequently one-minute electrocardiograms were taken. The results were quite uniform. From ten to fifteen minutes after the injection the ventricular rate began to increase and premature contractions began to diminish, the maximum effect being obtained in about thirty to forty-five minutes. At this point the premature contractions were either entirely, or almost entirely, absent and the ventricular rate rapid, 100 to 160 per minute. Within three to four hours this effect of atropine had completely disappeared, the heart resuming its previous slow rate with coupled rhythm. In the patient, previously discussed, in whom digitalis gave rise to marked irregularities in ventricular complexes resembling a prefibrillary state of the ventricle, 4 milligrams of atropine abolished temporarily all aberrant beats. Although it was not done in this case, it seems justifiable to raise the question whether by the repeated administration of the atropine the abnormal state induced in the ventricle might not be held in abeyance so that sufficient elimination can take place for the heart to recover from the more severe toxic effect of the digitalis.

SUMMARY AND CONCLUSIONS

1. An analysis of a series of 86 patients with auricular fibrillation receiving digitalis shows that nearly all such patients at some time have premature contractions of ventricular origin.

2. The premature contraction occurring spontaneously or as a result of digitalis does not signify susceptibility to digitalis bigeminy.

3. The evidence at hand lends no support to the idea that susceptibility to the coupled rhythm depends upon the prolonged use of digitalis.

4. Digitalis bigeminy in our cases was seen six times as often in patients with auricular fibrillation as in those with a regular sinus rhythm.

5. Digitalis bigeminy occurs in patients of all ages and in all etiological and pathological types of heart disease, but, in our cases, was seen relatively more frequently both in patients below the age of forty years and in those with rheumatic heart disease.

6. The duration of digitalis bigeminy after withdrawal of the drug varies with different patients and at different times in the same pa-

tient. The duration of the bigeminy in some patients becomes longer as the myocardial failure increases.

7. In patients susceptible to digitalis bigeminy, the margin of safety between functional improvement and the inception of the toxic rhythm varies. A possible danger has been pointed out in the treatment with digitalis of those patients in whom functional improvement occurs only with those doses that call forth a coupled rhythm.

8. The subcutaneous administration of 4 milligrams of atropine sulphate in 5 patients acted uniformly in affecting either a marked reduction or complete abolition of the coupled rhythm.

9. Patients susceptible to digitalis coupling fall into two general classes from the functional standpoint: (1) those in whom it appears hand in hand with increasing myocardial failure and (2) those who have relatively good myocardial power and in whom it appears without any change in the functional capacity of the heart. There is another group of patients in whom susceptibility to bigeminy develops or is increased during acute infection.

10. The prognosis in patients in whom digitalis bigeminy occurs is, in general, poor. But the evidence at hand does not justify the conclusion that susceptibility to bigeminy indicates grave prognosis beyond that obtained from the functional capacity of the heart.

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EXPERIMENTAL HEART DISEASE*

II. The Effect of Experimental Aortic Regurgitation on the Heart Weights; with a Consideration of Some Factors Concerned in Cardiac Hypertrophy and a Summary of the Manifestations of Exerimental Heart Disease

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THE problem of the factors concerned in the production of cardiac hypertrophy is still an unsolved one in spite of the mass of exhaustive experimental work. The data that is about to be presented does not solve the problem, but it does throw light upon some of the factors that determine the location, the degree and the character of the enlargement of the heart. This study was first undertaken to determine the effect of various degrees of hypertrophy upon the electrocardiogram. As this point was established, other more fundamental facts were observed and interest was aroused in the whole broad problem of cardiac hypertrophy and also in the manifestations of experimental heart disease.

Experimental aortic regurgitation was first produced by Becker[1] in the early seventies. This experimenter introduced a glass rod down the dog's carotid and ruptured the aortic cusps in order to study the effect of the valve lesion on the pulse in the retinal arteries. He made no observations as to any other effects of the lesion on the circulation.

Cohnheim[2] performed similar experiments and observed especially the effect of aortic regurgitation on the general arterial pressure. Klebs[3] extended the observations to include the effects of mitral regurgitation, which he was able to produce in the dog by means of a specially constructed instrument. Rosenbach[4] concluded from his experimental studies that in experimental aortic regurgitation the blood pressures did not return toward the normal levels and that the heart compensated first by dilatation and later by hypertrophy. Tangl[5] produced aortic regurgitation in rabbits and studied the hypertrophied left ventricle microscopically.

Hasenfeld and Romberg[6] established a small control series for the weights and ratios of rabbits' hearts divided by the method of Müller.

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They then divided the hearts of a series of rabbits that had had experimental aortic regurgitation for varying periods of time (95 to 128 days). Varying degrees of left ventricular hypertrophy were noted in this small series, and attributed to the varying degrees of aortic regurgitation. Bálint's[7] experiments with dogs, cats and rabbits seemed to confirm the fact that the hypertrophy stood in direct relation to the increase in work resulting from the defective valve. Stadler,[8] like Tangl and others, studied the microscopic effects of experimental aortic regurgitation.

Stewart[9] established a control series of twenty dogs, the hearts of which were divided by the obsolete Müller's method. He then produced aortic regurgitation in a small series of dogs by cutting the posterior aortic cusp with a valvulotome, and studied the effects. Of his twenty dogs, six had the lesion for five to seven days; six for eleven to twenty days; six for twenty-one to twenty-eight days; one for fifty-six and one for one hundred and twenty days. Proportional weights alone were calculated and it was noted that there was apparently as much hypertrophy at the end of the first week as was present at the end of the second week, but that there was an increase with the beginning of the third week. I calculated the L/R ratios from the figures given and found them to range from 2.150 to 3.720 with an average of 2.750. These ratios I note are at considerable variance with the proportional ratios which Stewart used, with higher figures in cases which showed little or no hypertrophy in the proportional weight and lower figures in the cases with the higher proportional weights. These discrepancies emphasize the inaccuracies of the Müller method. The total heart weight body weight ratio, H.W./B.W., varied from .00678 to .01373, with an average of .01010. The left ventricular weight body weight ratio, L.V.W./B.W., varied from .00382 to .00718, with an average of .00501. The right ventricular weight body weight ratio, R.V.W./B.W., varied from .00004 to .00249, with an average of .00175. The septum weight body weight, S.W./B.W., varied from .00135 to .00297 with an average of .00222. The total ventricular weight body weight ratio, T.V.W./B.W., varied from .00726 to .01242, with an average of .00903. Variances such as those mentioned in the L/R ratios were also noted to a somewhat lesser extent in the proportional ratios. Stewart concluded that the hypertrophy of experimental aortic regurgitation involves all chambers of the heart. The greatest absolute increase in weight was in the left ventricle. The remaining segments arranged in the order of decreasing increments were septum, right ventricle and auricles. The left ventricle showed the greatest relative increase, while the auricles were next in order in this respect. The auricular hypertrophy was due in Stewart's opinion to increased force of auricular systole and not due to altered venous pressure.

THE GENESIS AND NATURE OF CARDIAC HYPERTROPHY

Increased work has been generally considered to be the stimulus and main factor concerned in hypertrophy of the heart ever since the studies of Corvisart[10] on cardiac valvular lesions, in 1806, and Traube's[11] studies, in 1856, on the relation of hypertonia to cardiac hypertrophy. Cohnheim,[2] in 1882, restated the work hypertrophy hypothesis very emphatically. Rosenbach[4] and also Thorel[12] considered, as a predisposing factor, but not as the cause of cardiac hypertrophy, the increased coronary flow with its accompanying increased nutrition which the increased activity of the muscle incurs. Koester[13] considered the prolongation of the mesosystolic period, with its cycle of prolonged hyperemia allowing a greater assimilation of nutritive substances, the factor of importance in the production of hypertrophy. Horvath[14] disagrees entirely with the theory that attributes hypertrophy to increased work. The stimulus to contraction, or the contraction itself, results in a stretching greater than normal with the demand for increased work. This contention he based on the physiological law that muscles perform work in proportion to the degree to which they are stretched. This stretching excites increased contraction and also increased growth, thus acting as a common etiological factor of both work and of hypertrophy, which are not to be considered as related in the sense of cause and effect. In support of this hypothesis, Horvath cites analogous instances of the lack of relation between size of organ and the amount of work it performs as in the case of the diaphragm and the masseters. The uterus he considers as further support of his hypothesis since it hypertrophies during pregnancy, yet in his opinion, no work is accomplished during this time. Albrecht[15] interpreted cardiac hypertrophy in the light of his microscopic findings, which suggested a lesion of an inflammatory nature similar to that found by Virchow in the hypertrophic conditions of the liver cells in the early stage of inflammation. He found uniformly an increase in the amount of connective tissue, vacuolization of the muscle cells, enlargement of the muscle fiber, due entirely to the increase in sarcoplasm, and no increase in the fibrillae or contractile elements. Aschoff[16] considered the data for this unreliable. Stadler[8] found enlargement of the fibrillae. Albrecht also described degeneration of the anisotropic and increase in the isotropic elements of the cell, and a frequent doubling of the nuclei. On the basis of his microscopic findings he insisted that hypertrophy is not a compensatory process. He pointed out that in idiopathic hypertrophy no mechanical explanation can be found to account for the enormous hypertrophy, while in valvular defects the hypertrophy is usually not so extensive and is not confined to a part that bears the brunt of the excessive work.

Tangl,[5] Hasenfeld,[6] and Bálint[7] found no increase in connective tissue in the early stages of hypertrophy after experimental valve lesion. Letulle[17] considered two stages in the progress of cardiac hypertrophy: the first a period of progressive increase in the nutritional state in which the muscle fibers lengthen and thicken and the second a period of disturbed nutrition with degeneration of the muscle fibers and at the same time, an increase in the interstitial tissue. Dehio[18] emphasized the point that it is only in the late stages, with high grade hypertrophy and the signs of stasis, motor insufficiency and cardiac dilatation, that the connective tissue undergoes hypertrophic proliferation. In other words, any factor that leads to an overstretching of the heart muscle and dilatation of the cavities gives the stimulus to an increase of interstitial connective tissue. The increased intracardial diastolic blood pressure in dilatation produces stasis in the capillaries of the myocardium, which stasis predisposes to further induration. Stadler's[8] findings, especially after experimental tricuspid insufficiency, agreed with this idea. Virchow[19] considered the basis of the later lesions to be the "parenchymatous inflammation," the result of nutritional disturbances, and the result of an increased intake of material into the cell and indistinguishable from early hypertrophy, both conditions presenting the microscopic picture of cloudy swelling.

The microscopic studies of Goldenberg,[20] Tangl,[5] Dehio[18] and Stadler,[8] with those of Richard M. Pearce,[21] and of Karsner, Saphir and Todd,[22] all agree that in cardiac hypertrophy the heart muscle cells enlarge and account for the increase in size of the heart and that no multiplication of heart muscle fibers is present. The swelling of the individual heart muscle fibers is theoretically accounted for on the physicochemical basis that Loeb[23] and Cooke[24] described for skeletal muscle hypertrophy. Heavy muscular work results in a breaking down of complex protein molecules into simpler ones, thus increasing the intracellular molecular concentration of the muscle plasma, producing a rise in the osmotic pressure; and endosmosis which results in a swelling of the muscle cell.

Lewis and Drury[26] in connection with work on arteriovenous aneurysm have suggested as a cause for the cardiac enlargement (which in arteriovenous anastomosis they considered primarily and chiefly a dilatation) a deficient nutrition of the heart muscle due to a deficient coronary flow consequent on the fall of mean arterial pressure. They further state that a deficient supply of oxygenated blood to the coronary vessels is probably the cause, or a contributing cause, of cardiac enlargement in such conditions as aortic regurgitation, decrease in the caliber of the coronary arteries, anemia and any condition in which the output of the heart is decreased or the mean arterial pressure is much reduced.

There is thus no general agreement as to the primary factor concerned in cardiac hypertrophy. In the vain attempts to fix one factor as the primary factor, sight seems to have been lost of the possibility of combination of factors. Furthermore, clinical medicine has recognized contributory factors which in a large measure determine the degree or extent of the hypertrophy. Our experimental studies have yielded data substantiating some of the clinical opinions as to important contributory factors.

THE EXPERIMENTAL PROCEDURE

Control electrocardiograms in the three standard leads were taken with the dogs lying squarely on their backs, first awake and later completely anesthetized with ether. Control x-ray films of the heart at a distance of five feet were also taken in many instances. Control blood pressure curves were traced in some cases and control blood volume estimations were attempted in a few dogs. The valve areas over the precordium were carefully auscultated to be sure that no murmurs were present to start with.

The neck of the anesthetized dog was prepared as for a surgical operation, shaved and cleansed. With aseptic technic the left carotid artery was exposed and a valvulotome introduced. (Fig. 3.) The head of the instrument was passed downward carefully until the valvular resistance of the aortic cusps was met. The posterior aortic sinus of Valsalva was usually entered and the head of the valvulotome, directed by a blunt pyramid at its anterior inferior border, was thrust through the posterior aortic cusp into the lumen of the aortic ring. The valvulotome was drawn back slightly and the valve sail was caught in the hook, the inside of which is a sharpened knife edge. In the withdrawal of the valvulotome, the aortic cusp was cut or torn and an aortic regurgitation resulted. The type and extent of the lesion was by no means always the same, as may be readily seen in Fig. 4. Uniformity in extent would be quite desirable, but is unobtainable in adult dogs by this more or less blind method. It is usually possible to select the posterior cusp for traumatization. This posterior cusp lesion is preferable, since there is no coronary artery arising from the posterior sinus and consequently little danger of disastrous interference with the coronary circulation.

The left carotid artery was ligated* and the wound carefully closed.

The acute traumatic aortic regurgitation was accompanied by the water-hammer pulse, a high pulse pressure, throbbing peripheral vessels with a pistol-shot sound and a Duroziez's diastolic murmur in the compressed femoral artery. The capillary pulse did not appear at once but usually was elicited later. The pulsation appeared in the ret-

*The vertebral arteries of the dog are of such a caliber that the ligation of one carotid produces no significant disturbance.

inal arteries quite promptly. The aortic diastolic murmurs appeared immediately, but seemed to increase in intensity with time but sometimes there was a decrease. As shown in Fig. 4, the damaged valves healed and in time became thickened and stiffened with scar tissue.

Electrocardiograms were taken immediately after operation and again at weekly and monthly intervals thereafter and whenever the dog appeared sick and just before a dog was sacrificed. X-ray films of the heart and blood pressure curves were also made at intervals and before final fatal anesthetization.

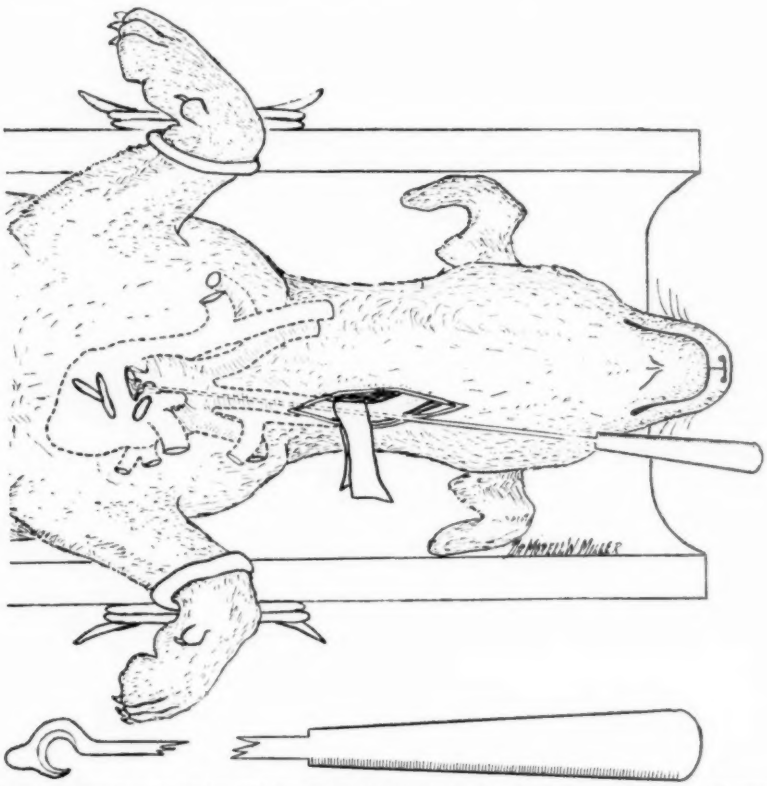

Fig. 3.—Drawing to show the technic of the operation for the production of experimental aortic regurgitation. Below is an enlarged drawing of the especially modified valvulotome.

After the recovery from the operation, the dogs were transferred to the kennels, which at first were covered damp pens about three meters square but later consisted of a house of this size and a run about seven and a half meters square. Some dogs were restricted by a two meter chain.

The dogs that died at operation were used as normals and electrocardiographic controls. The hearts were sectioned and recorded as described in the preceding paper. The dogs that showed no murmurs or vascular signs were sacrificed at varying intervals, the hearts

studied as outlined previously, and used as electrocardiographic and operated controls.

The dogs presenting the signs of aortic regurgitation were sacrificed following the recording of final observations and curves, at the end of varying intervals from 2 to 530 days after the operation at which the lesion was produced. The hearts were all sectioned according to the author's method and Lewis' method and the proportional weights and ratios calculated and recorded.

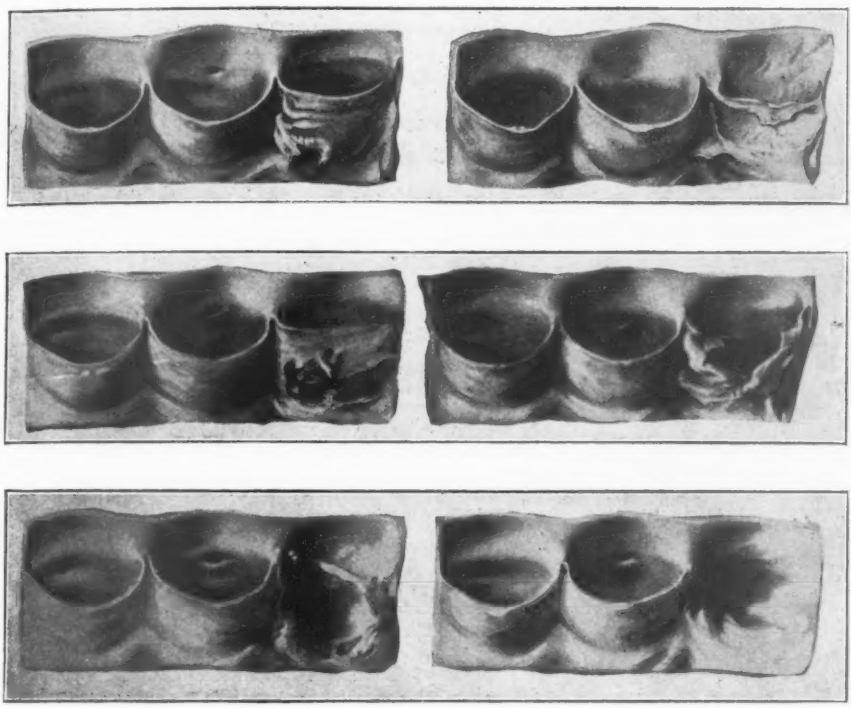

Fig. 4.—Drawings of the aortic cusps of six dogs that had survived the operation in which the posterior cusps were damaged. The varying degrees of damage to the posterior cusps are evident.

THE RESULTS OF THE EXPERIMENTAL AORTIC REGURGITATION

One hundred and fifty dogs were operated upon. Thirty-five dogs died at operation or within twenty-four hours after operation. Of those that survived the operation, thirty presented no evidences of aortic regurgitation. At autopsy at varying intervals after operation, no valve lesions, but scars in the posterior aortic sinus and often also in the interventricular septum, were found. Ten of the dogs operated upon presented atypical aortic regurgitant murmurs and were found to have perforations of the aortic root, with a sinus leading from the floor of the posterior aortic sinus into the right heart.

Seventy-five dogs presented the typical signs of aortic regurgita-

TABLE V

DATA ON DOGS SHOWING NO CONSPICUOUS LEFT VENTRICULAR HYPERTROPHY

(0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
						AUTHOR'S METHOD			LEWIS' METHOD												
INTERVAL IN DAYS	BODY WT. IN KG.	FRESH TOTAL HEART WT. IN GMS.	FRESH AUR. WT.	FRESH VENT. WT.	CLEAN AND FIXED VENT. WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	SEPTUM WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	RATIO TOTAL HT. WT. BD. WT.	FRESH AUR. WT. BD. WT.	FRESH VENT. WT. BD. WT.	CLEAN AND FIXED VENT. WT. BD. WT.	H. L. VENT. BD. WT.	H. R. VENT. BD. WT.	L. SEPTUM BD. WT.	L. L. VENT. BD. WT.	L. R. VENT. BD. WT.
Data on 10 Dogs with Perforation of Aortic Root																					
23	13. k	97.	10.	87.	80.	47.	33.	1.425	13.	41.	26.	1.577	.00746	.00077	.00670	.00615	.00361	.00254	.00100	.00315	.00200
30	6. k	62.	7.	55.	46.	28.	18.	1.556	85.	23.	14.5	1.588	.01032	.00117	.00916	.00767	.00467	.00300	.00142	.00384	.00242
30	20. k	178.	18.	160.	145.	82.	63.	1.300	25.	68.	52.	1.310	.00890	.00090	.00800	.00725	.00410	.00315	.00125	.00340	.00260
38	14.1k	144.	15.	129.	100.	60.	40.	1.500	16.	51.	33.	1.545	.01021	.00107	.00915	.00710	.00425	.00284	.00113	.00362	.00234
54	18. k	134.	19.	115.	96.	57.	39.	1.460	17.	47.	32.	1.470	.00745	.00106	.00638	.00533	.00317	.00217	.00094	.00261	.00178
60	13.7k	113.	12.	101.	85.	50.	35.	1.428	17.	40.	28.	1.428	.00825	.00088	.00737	.00620	.00365	.00256	.00124	.00292	.00210
130	21.7k	166.	18.	148.	139.	83.	56.	1.482	30.	67.	42.	1.595	.00766	.00083	.00682	.00641	.00382	.00258	.00138	.00309	.00194
156	10.5k	112.	9.	103.	95.	55.	40.	1.375	19.	46.	30.	1.533	.01068	.00086	.00980	.00905	.00524	.00381	.00181	.00438	.00286
380	11.6k	117.	11.	106.	90.	51.	39.	1.310	16.	42.	32.	1.312	.01010	.00095	.00914	.00776	.00440	.00336	.00138	.00362	.00276
460	10.8k	111.	10.	101.	94.	52.	42.	1.238	15.	45.	34.	1.288	.01028	.00093	.00935	.00870	.00482	.00389	.00139	.00417	.00315
Data on 30 Dogs With Aortic Regurgitation and No Conspicuous Left Ventricular Hypertrophy																					
2	5. k	47.	4.	43.	37.	22.	15.	1.467	7.	18.	12.	1.500	.00940	.00080	.00860	.00740	.00440	.00300	.00140	.00360	.00240
3	8.2k	74.	9.	65.	54.	33.	21.	1.571	11.	27.	16.	1.678	.00903	.00110	.00793	.00659	.00403	.00256	.00134	.00329	.00195
4	9.5k	92.	10.	82.	71.	44.	27.	1.630	13.	37.	21.	1.760	.00968	.00105	.00863	.00747	.00463	.00284	.00137	.00390	.00221
5	4.6k	36.	5.	31.	28.	18.	10.	1.800	5.	15.	8.	1.875	.00783	.00109	.00675	.00609	.00391	.00217	.00109	.00326	.00174
6	5.3k	45.	5.	40.	37.	21.	16.	1.312	8.	17.	12.	1.418	.00850	.00094	.00755	.00699	.00396	.00302	.00151	.00321	.00226

TABLE V—CONT'D

(0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
8	3.6k	37.	5.	32.	28.	17.	11.	1.546	6.	14.	8.	1.750	.01028	.00139	.00890	.00778	.00472	.00306	.00167	.00389	.00222
10	13.3k	129.	17.	112.	99.	60.	39.	1.540	17.	51.	31.	1.645	.00970	.00128	.00842	.00745	.00451	.00293	.00128	.00384	.00233
12	11.5k	107.	13.	94.	80.	48.	32.	1.500	15.	40.	25.	1.600	.00930	.00113	.00816	.00696	.00417	.00278	.00130	.00348	.00217
12	9.2k	92.	9.	83.	79.	48.	31.	1.548	14.	40.	25.	1.600	.01000	.00098	.00902	.00859	.00522	.00337	.00152	.00435	.00272
14	23. k	205.	33.	172.	147.	89.	58.	1.535	27.	75.	45.	1.666	.00891	.00144	.00748	.00640	.00387	.00252	.00117	.00326	.00196
14	7.5k	61.	9.	52.	49.	28.	21.	1.333	9.	23.	17.	1.352	.00813	.00120	.00694	.00654	.00374	.00280	.00120	.00307	.00227
16	3.5k	39.	7.	32.	27.5	17.	10.5	1.620	7.5	13.	7.	1.886	.01114	.00200	.00915	.00786	.00486	.00300	.00214	.00372	.00200
18	9. k	72.	6.	66.	62.	37.	25.	1.481	14.	30.	18.	1.668	.00800	.00067	.00734	.00689	.00411	.00278	.00156	.00334	.00200
21	9.8k	78.	7.	71.	62.	38.	24.	1.583	13.	31.	18.	1.722	.00796	.00071	.00725	.00633	.00388	.00245	.00133	.00316	.00184
23	16.5k	178.	18.	160.	147.	90.	57.	1.578	25.	78.	44.	1.772	.01079	.00109	.00970	.00891	.00545	.00346	.00152	.00473	.00267
24	9. k	87.	8.	79.	70.	40.	30.	1.333	11.	34.	25.	1.360	.00966	.00089	.00878	.00778	.00445	.00334	.00122	.00378	.00278
24	6.8k	59.	7.	52.	47.	30.	17.	1.765	9.	25.	13.	1.922	.00868	.00103	.00765	.00691	.00441	.00250	.00132	.00368	.00191
28	7.8k	62.	7.	55.	48.	30.	18.	1.667	8.	26.	14.	1.857	.00795	.00090	.00705	.00616	.00385	.00231	.00103	.00356	.00180
30	7.2k	72.	7.	65.	51.	31.	20.	1.550	10.	25.	16.	1.560	.01000	.00097	.00903	.00708	.00431	.00278	.00139	.00347	.00222
52	10.5k	109.	11.	98.	85.	51.	34.	1.500	14.	44.	27.	1.630	.01038	.00105	.00933	.00810	.00485	.00324	.00133	.00419	.00257
56	19.8k	234.	24.	210.	175.	107.	68.	1.574	28.	95.	56.	1.696	.01181	.00121	.01060	.00884	.00540	.00344	.00141	.00480	.00282
100	12. k	155.	22.	133.	113.	65.	48.	1.354	16.	57.	40.	1.425	.01292	.00183	.01110	.00942	.00541	.00400	.00133	.00475	.00333
114	10. k	96.	13.	83.	76.	44.	32.	1.375	13.	37.	24.	1.582	.00960	.00130	.00830	.00760	.00440	.00320	.00130	.00370	.00240
150	8.5k	86.	8.	78.	74.	47.	27.	1.740	15.	38.	21.	1.810	.01011	.00094	.00917	.00871	.00553	.00318	.00177	.00447	.00247
152	11.7k	135.	10.	125.	117.	69.	48.	1.438	17.	59.	41.	1.440	.01152	.00085	.01070	.01000	.00590	.00410	.00145	.00505	.00350
156	6.8k	59.	7.	52.	48.	30.	18.	1.666	11.	24.	13.	1.846	.00868	.00103	.00765	.00706	.00441	.00265	.00162	.00353	.00191
202	11.4k	87.	8.	79.	69.	43.	26.	1.652	13.	36.	20.	1 800	.00764	.00070	.00693	.00695	.00377	.00228	.00114	.00316	.00175
208	15.4k	145.	13.	132.	112.	70.	42.	1.668	20.	60.	32.	1.818	.00942	.00084	.00858	.00727	.00455	.00273	.00130	.00389	.00208
300	13.3k	113.	13.	100.	92.	56.	36.	1.555	18.	46.	28.	1.642	.00850	.00098	.00752	.00692	.00421	.00271	.00135	.00346	.00210
452	14.4k	133.	12.	121.	113.	69.	44.	1.570	21.	57.	35.	1 627	.00924	.00083	.00840	.00785	.00479	.00306	.00146	.00396	.00243

TABLE VI

DATA ON 40 DOGS WITH AORTIC REGURGITATION AND DEFINITE LEFT VENTRICULAR HYPERTROPHY

(0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
						AUTHOR'S METHOD				LEWIS' METHOD											
INTERVAL IN DAYS	BODY WT. IN KG.	FRESH TOTAL HEART WT. IN GMS.	FRESH AUR. WT.	FRESH VENT. WT.	CLEAN AND FIXED VENT. WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	SEPTUM WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	RATIO TOTAL HT. WT. BD. WT.	FRESH AUR. WT. BD. WT.	FRESH VENT. WT. BD. WT.	CLEAN AND FIXED VENT. WT. BD. WT.	H. L. VENT. BD. WT.	H. R. VENT. BD. WT.	L. SEPTUM BD. WT.	L. L. VENT. BD. WT.	L. R. VENT. BD. WT.
19	5. k	56.	6.	50.	45.	30.	15.	2.000	7.	26.	12.	2.162	.01120	.00120	.01000	.00900	.00600	.00300	.00140	.00520	.00240
20	12.8	130.	13.	117.	111.	73.	38.	1.920	19.	62.	30.	2.066	.01016	.00102	.00915	.00867	.00570	.00297	.00148	.00485	.00234
20	6.3k	63.	8.	55.	46.	31.	15.	2.066	8.	26.	12.	2.166	.01000	.00127	.00873	.00730	.00492	.00238	.00127	.00413	.00191
22	4.5k	45.	5.	40.	38.	25.	13.	1.922	8.	20.	10.	2.000	.01000	.00111	.00890	.00845	.00556	.00289	.00178	.00445.	.00222
22	3.7k	37.	5.	32.	31.	21.	10.	2.100	5.	18.	8.	2.315	.01000	.00135	.00865	.00838	.00568	.00270	.00135	.00486	.00216
24	6. k	60.	6.	54.	45.	30.	15.	2.000	8.	25.	12.	2.082	.01000	.00100	.00900	.00750	.00500	.00250	.00133	.00417	.00200
30	2.5k	28.	3.	25.	22.	15.	7.	2.140	4.5	13.	5.5	2.362	.01120	.00120	.01000	.00880	.00600	.00280	.00180.	.00520	.00220
42	11. k	117.	11.	106.	98.	65.	33.	1.970	17.	56.	25.	2.240	.01063	.00100	.00963	.00891	.00591	.00300	.00155	.00509	.00227
50	7.2k	72.	7.	65.	54.	36.	18.	2.000	10.	30.	14.	2.141	.01000	.00097	.00903	.00750	.00500	.00250	.00139	.00417	.00194
60	8. k	80.	9.	71.	67.	46.	21.	2.300	11.	40.	16.	2.500	.01000	.00112	.00888	.00837	.00575	.00262	.00137	.00500	.00200
60	9.6k	108.	12.	96.	83.	58.	25.	2.320	13.	50.	20.	2.500	.01126	.00125	.01000	.00865	.00605	.00261	.00135	.00521	.00208
70	11.5k	131.	11.	120.	112.	72.	40.	1.800	22.	61.	29.	2.100	.01139	.00096	.01042	.00974	.00626	.00348	.00191	.00530	.00252
70	12.7k	160.	14.	146.	137.	93.	44.	2.106	22.	80.	35.	2.282	.01260	.00110	.01150	.01078	.00732	.00346	.00173	.00630	.00276
72	7.8k	92.	12.	80.	78.	54.	24.	2.250	10.	48.	20.	2.400	.01180	.00154	.01027	.01000	.00693	.00308	.00128	.00615	.00256
80	6.8k	77.	7.	70.	64.	44.	20.	2.200	10.	38.	16.	2.375	.01132	.00103	.01030	.00942	.00647	.00294	.00147	.00560	.00236

TABLE VI—CONT'D

(0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
88	10. k	105.	11.	93.	69.	46.	23.	2.000	12.	47.	20.	2.350	.01050	.00110	.00930	.00690	.00460	.00230	.00120	.00470	.00200
90	9.3k	94.	10.	84.	76.	52.	24.	2.166	14.	43.	19.	2.262	.01010	.00108	.00904	.00817	.00560	.00258	.00151	.00462	.00204
96	6. k	66.	7.	59.	53.	37.	16.	2.306	11.	30.	12.	2.500	.01100	.00117	.00984	.00884	.00617	.00267	.00183	.00500	.00200
100	4.8k	60.	6.	54.	46.	32.	14.	2.283	11.	24.	10.	2.400	.01250	.00125	.01125	.00958	.00677	.00292	.00250	.00500	.00208
102	4. k	54.	4.	50.	46.	31.	15.	2.068	11.	24.	11.	2.181	.01350	.00100	.01250	.01150	.00775	.00375	.00275	.00600	.00275
110	3. k	38.	3.	35.	32.	22.	10.	2.200	6.	18.	8.	2.250	.01267	.00100	.01167	.01068	.00734	.00333	.00200	.00600	.00267
124	10.8k	150.	16.	134.	121.	78.	43.	1.800	20.	69.	34.	2.015	.01389	.00148	.01240	.01120	.00722	.00398	.00185	.00639	.00315
126	7. k	70.	7.	63.	58.	38.	20.	1.900	12.	32.	14.	2.284	.01000	.00100	.00900	.00829	.00543	.00286	.00171	.00457	.00200
128	8. k	88.	10.	78.	74.	50.	24.	2.082	14.	42.	18.	2.332	.01100	.00125	.00975	.00925	.00625	.00300	.00175	.00525	.00225
132	8.6k	132.	14.	118.	106.	70.	36.	1.942	20.	60.	26.	2.384	.01535	.00163	.01371	.01233	.00814	.00418	.00233	.00698	.00302
134	12.4k	132.	14.	118.	116.	78.	38.	2.052	21.	65.	30.	2.168	.01064	.00113	.00951	.00936	.00628	.00306	.00169	.00524	.00242
136	12.2k	132.	17.	115.	99.	68.	31.	2.194	16.	60.	23.	2.604	.01082	.00139	.00943	.00811	.00557	.00254	.00131	.00492	.00189
140	8. k	102.	11.	91.	84.	60.	24.	2.500	16.	51.	17.	3.000	.01275	.00138	.01138	.01050	.00750	.00300	.00200	.00638	.00213
144	5.5k	67.	5.	62.	56.	38.	18.	2.106	9.	33.	14.	2.358	.01219	.00091	.01128	.01018	.00691	.00328	.00164	.00618	.00255
150	10.5k	123.	11.	112.	105.	71.	35.	2.028	19.	60.	25.	2.400	.01172	.00105	.01066	.01000	.00676	.00333	.00181	.00571	.00238
156	7. k	70.	9.	61.	56.	37.	19.	1.948	10.	31.	15.	2.066	.01000	.00129	.00872	.00800	.00529	.00272	.00143	.00443	.00214
162	10.7k	123.	11.	112.	103.	68.	35.	1.942	22.	54.	27.	2.000	.01150	.00103	.01047	.00964	.00635	.00327	.00206	.00505	.00252
168	12. k	120.	10.	110.	98.	68.	30.	2.266	18.	57.	23.	2.480	.01000	.00083	.00917	.00816	.00566	.00250	.00150	.00475	.00192
170	6.5k	91.	9.	82.	74.	50.	24.	2.082	10.	45.	19.	2.368	.01384	.00138	.01260	.01138	.00770	.00370	.00154	.00693	.00292
176	7.1k	75.	10.	65.	62.	41.	21.	1.952	15.	32.	15.	2.132	.01056	.00141	.00916	.00874	.00577	.00296	.00211	.00450	.00211
186	10. k	102.	10.	92.	83.	55.	27.	2.018	16.	45.	21.	2.142	.01020	.00100	.00920	.00830	.00550	.00270	.00160	.00450	.00210
200	14.3k	160.	18.	142.	138.	89.	49.	1.818	27.	75.	36.	2.022	.01119	.00126	.00993	.00965	.00622	.00342	.00189	.00525	.00252
210	13.2k	154.	12.	142.	113.	76.	37.	2.052	21.	65.	27.	2.402	.01168	.00091	.01076	.00856	.00575	.00280	.00159	.00493	.00202
345	14. k	140.	13.	127.	124.	84.	40.	2.100	26.	68.	30.	2.266	.01000	.00093	.00907	.00886	.00600	.00286	.00186	.00486	.00214
530	16. k	222.	17.	205.	197.	130.	67.	1.942	32.	113.	50.	2.260	.01388	.00106	.01280	.01231	.00813	.00418	.00200	.00706	.00312

tion. Five of these are still living. Thirty of these had hearts that showed no conspicuous preponderant hypertrophy, while forty showed definite preponderant hypertrophy of the left ventricle. Table V contains the data on the ten dogs that had perforation of the aortic root, followed by the data on the thirty dogs that showed no conspicuous preponderant hypertrophy. Table VI contains the data on the forty dogs that showed preponderant left ventricle hypertrophy.

The columns of data in these tables correspond to those of the normals in the preceding paper except that a zero (0) column is added in which the time interval that has elapsed since operation is indicated in days. Each group is arranged with the data of the shortest interval at the top and that of the longest at the bottom of the column. In order from left to right the columns contain:

(1) Body weight of the dogs in kilograms;
(2) Total fresh heart weight in grams;
(3) Fresh auricular weight in grams;
(4) Fresh ventricular weight in grams;
(5) Cleaned and fixed ventricular weight in grams;
(6) Left ventricular weight in grams, after separation by author's method;
(7) Right ventricular weight in grams, after separation by author's method;
(8) Ratio of left ventricular weight to right ventricular weight, after separation by author's method.
(9) Septal weight, after separation by Lewis' method.
(10) Left ventricular weight, after separation by Lewis' method;
(11) Right ventricular weight, after separation by Lewis' method;
(12) Ratio of left ventricular weight to right ventricular weight, after separation by Lewis' method.
(13) Ratio of the total fresh heart weight to the body weight;
(14) Ratio of the fresh auricular weight to the body weight;
(15) Ratio of the fresh ventricular weight to the body weight;
(16) Ratio of the cleaned and fixed ventricular weight to the body weight, which is the same as the cleaned fresh, since the weight after fixation is brought back to the fresh weight;
(17 Ratio of the left ventricular weight, after separation by the author's method, to the body weight;
(18) Ratio of the right ventricular weight, after separation by the author's method, to the body weight;
(19) Ratio of the septal weight after separation by Lewis' method to the body weight;
(20) Ratio of the left ventricular weight after separation by Lewis' method, to the body weight;
(21) Ratio of the right ventricular weight, after separation by Lewis' method, to the body weight.

RELATION OF DEGREE OF HYPERTROPHY TO THE DURATION OF THE LESION

A glance at the tables will convince one that the duration of the lesion is not the chief factor concerned in hypertrophy, though it does play a part. In the ten instances in which perforation of the aortic root was found, only those five that had existed for more than

TABLE VII

RELATION OF EXTENT OF HYPERTROPHY TO DURATION OF THE EXPERIMENTAL AORTIC REGURGITATION

RATIOS INTERVALS IN DAYS NUMBER OF DOGS IN SERIES	(1) L/(H) /R	(2) % INCREASE	(3) L/(L) /R	(4) % INCREASE	(5) H.W./ /B.W.	(6) % INCREASE	(7) L.V.W./(H) /B.W.	(8) % INCREASE	(9) L.V.W./(L) /B.W.	(10) % INCREASE
Normal Controls 200 dogs	1.393	0%	1.461	0%	.00798	0%	.00369	0%	.00306	0%
2 to 15 days 10 dogs	1.545	11%	1.649	13%	.00926	16%	.00434	18%	.00361	18%
15 to 30 days 15 dogs	1.728	24%	1.860	27%	.00958	20%	.00460	25%	.00401	31%
30 to 60 days 7 dogs	1.971	41%	2.153	47%	.01075	31%	.00557	51%	.00481	57%
70 to 110 days 10 dogs	2.053	47%	2.228	53%	.01176	47%	.00633	72%	.00534	75%
110 to 145 days 10 dogs	2.013	44%	2.298	57%	.01189	49%	.00650	76%	.00561	83%
150 to 185 days 10 dogs	1.908	37%	2.068	42%	.01081	36%	.00589	60%	.00489	60%
200 to 530 days 8 dogs	1.795	29%	1.950	33%	.01019	28%	.00543	47%	.00457	49%

thirty days showed hypertrophied hearts. These showed an increased tendency toward right ventricular preponderance, with increasing time interval, especially after 156, 380 and 460 days.

Of the thirty dogs with no preponderant hypertrophy, ten had had lesions for only 2 to 14 days; ten for 16 to 56 days; and ten for 100 to 452 days. The total heart weight body weight ratios indicated hypertrophy in only two pups in the 2 to 14 day group; five dogs in the 16 to 56 day group; and five in the 100 to 452 day group.

Of the forty dogs that showed definite preponderant left ventricular hypertrophy, only one dog with a lesion for less than 20 days (a young adult dog with a free aortic regurgitation for 19 days) showed an L/R ratio of 2.000 or more. A hurried survey of the columns shows no further striking relationship between L/R ratio and duration of lesion. In this group the H.W./B.W. ratio is regularly above .01000, which indicates some general hypertrophy.

Table VII, a condensed summary of the data from all of the 70 dogs that had had aortic regurgitation, shows more clearly the relation of the extent of hypertrophy to the duration of the experimental aortic regurgitation. In this table the more important averages are given for the 200 normal dogs and for seven groups of experimental dogs. The groups are made up of all dogs whose lesions have existed for the stated time interval. The averages of the important ratios for each group are recorded and compared with the normal average and the percentage of increase over the normal recorded. The columns in order contain the data as follows:

(1) L/R(H) is the ratio of the weight of the left ventricle to that of the right, after dissection by the author's method.

(2) The percentage increase of the average for the first ratio for the first group above the normal average.

(3) L/R(L) the same as 1, but after dissection by the Lewis method.

(4) The same as 2, but for the second or Lewis ratio.

(5) H. W./B. W. is the total fresh heart weight body weight ratio.

(6) The per cent increase of the heart weight body weight ratio for each group above that of the normal average ratio.

(7) L. V. W./B. W.(H) is the ratio of the left ventricular weight, after dissection by the author's method, to the body weight.

(8) The percentage increase of the above ratio over the normal average for this ratio.

(9) L. V. W./B. W.(L) is the same as 7, after the heart has been further divided by the Lewis method.

(10) The same as 8, but for the Lewis ratio.

The table shows a gradual increase in all the averaged ratios; this becomes conspicuous after thirty days and is maximum in the 70 to 110 day group. The maximum increases in the averages, for the ratios, fall between 50 and 75 per cent increases above the normal averages. After 110 days there is a gradual falling off in percentage.

TABLE VIII

COMPARISON OF HEART RATIOS IN NORMAL DOGS AND IN DOGS UNDER VARIOUS EXPERIMENTAL CONDITIONS

RATIOS NUMBER OF DOGS IN SERIES EXPERIMENTAL CONDITIONS	(1) L/(H) /R	(2) % INCREASE	(3) L/(L) /R	(4) % INCREASE	(5) H.W./ /B.W.	(6) % INCREASE	(7) L.V.W./(H) /B.W.	(8) % INCREASE	(9) L.V.W./(L) /B.W.	(10) % INCREASE
200 normal dogs	1.393	0%	1.461	0%	.00798	0%	.00369	0%	.00306	0%
Maximum in A. R. series	2.500	80%	3.000	105%	.01535	92%	.00814	112%	.00706	131%
70 dogs with aortic regurgitation	1.825	30%	2.018	45%	.01054	32%	.00550	49%	.00466	52%
40 dogs with A. R. with unilat. hypertrophy	2.071	49%	2.283	56%	.01133	42%	.00623	68%	.00527	72%
26 pups with A. R.	2.023	45%	2.208	51%	.01083	36%	.00577	56%	.00484	58%
44 adults with A. R.	1.743	25%	1.856	27%	.01035	30%	.00534	45%	.00451	46%
20 dogs with A. R. & endocarditis	1.959	41%	2.190	50%	.01120	40%	.00591	60%	.00504	65%
14 dogs with A. R. & spont. endocarditis	2.040	46%	2.288	57%	.01153	45%	.00628	70%	.00536	75%
8 dogs with A. R. + spartein & adrenalin	1.702	22%	1.871	28%	.00913	14%	.00458	24%	.00381	25%
10 dogs—perf. aortic root to rt. heart	1.407	1%	1.465	.3%	.00913	14%	.00417	13%	.00398	14%

This unexpected result is probably due to the fact that only the older dogs with the uninfected lesions survived for the longer periods of time. No significant increases in weight were noted in any hearts that had had valve lesions for any interval of less than nineteen days. This is contrary to the findings of Stewart, who reported changes within one week. I have not been able to produce significant changes in shorter time even in young dogs and with the help of infection. However, I hope to study this question further at some later date.

Beyond this establishment of a more or less minimum interval of eighteen days for definite hypertrophy to appear; and beyond a suggestion of a gradual rise to a maximum after an interval of about 110 days, we have no unquestionable evidence as to the absolute part that the duration of the lesion plays in the production of hypertrophy. The activity of the animal after the production of the lesion must be an important factor and should be more carefully evaluated, for a short interval in an active dog ought to be more effective than a longer interval in a sluggish dog. This point will be studied further at some future time.

THE RELATION OF THE DEGREE OF CARDIAC HYPERTROPHY TO VARIOUS EXPERIMENTAL CONDITIONS

In any long series of experiments, conditions are bound to vary and cognizance of the varying experimental conditions, and their bearing on the results obtained, often furnishes valuable clues to study in the solution of the problem. This is all the more true when one has a respectable group of experiments presenting each variation in the experimental conditions.

Table VIII contains the summarized data and group averages in eight variations in conditions that might be considered as factors influencing the degree of cardiac hypertrophy. The table is arranged just as the preceding one is, except that instead of averages of groups of dogs for varying time intervals, we have here the averages of groups under various experimental conditions. The vertical columns are numbered and labeled and contain the same type of ratios as those given in the preceding table. The values for the 200 normal dogs are repeated. The maximum values obtained, the averages for the seventy dogs with aortic regurgitation, and the average for the forty dogs with aortic regurgitation and conspicuous unilateral hypertrophy, are given along with their percentage increases above the normal average. It will be noticed that only in the single instance of the maximum value do the percentage increases approach even the lower limit of values as we encounter them in human cardiac hypertrophy (100 per cent to 500 per cent increases). In general, a 45 per cent to 65 per cent increase is a high value for experimental hypertrophy. This may be due to the relatively short period of existence

of the lesion in the life of the dog as compared with the part of the human life during which the cardiac valvular lesion is usually present.

The separation of the group of 70 dogs with aortic insufficiency into a group made up of all the pups (26) and a group comprised of all of the adult dogs (44) demonstrates very clearly that the youth of the dog is an important factor in the degree of hypertrophy produced. The pups showed almost twice as great a percentage increase in the L/R ratios as did the adult dogs, while the percentage increases in the other ratios were only from a fifth to a fourth greater in the pups. The reason for this is not apparent. The pups were simply much more prone to unilateral hypertrophy. The extent of the lesion may play a part in this, since as a rule greater lesions are produced in pups than in adult dogs. Furthermore, the pups are more likely to have a complicating spontaneous endocarditis than are adult dogs. In spite of these secondary factors the youth of the tissues is probably also a factor, but more data is required to fix this point.

That infection is an important factor in the production of cardiac hypertrophy is indicated in the relatively high percentage increase in the ratios of dogs with spontaneous endocarditis and endocarditis experimentally engrafted upon the traumatic valve lesion. The duration of the infection was usually only a matter of days. As a rule endocarditis proved fatal within ten days, and no dog lived more than fifteen days after the first evidence of indisposition was noticed. The infecting organisms were usually streptococci. The edema accompanying the infection may be the basis of some of the increase in weight of the left ventricle in an infected aortic insufficiency.

The hypertrophy of aortic insufficiency is most conspicuous in the left ventricle, as Table VII shows. The H.W./B.W. ratio, however, always showed absolute hypertrophy also and the A.W./B.W. and R.V.W./H.W. show that the other parts of the hearts also hypertrophy to some extent.

The injection into dogs with aortic valve lesions of spartein sulphate and adrenalin hydrochloride, in the hope of producing myocardial changes and greater hypertrophy, as Fleisher and Loeb[25] and Christian and Walker[27] succeeded in doing in the rabbit, was quite disappointing. The percentage increases were less than they should have been for the aortic regurgitation alone. Further studies are necessary in this direction, for it may be that toxic agents actually cause atrophic changes with little or no regeneration or hypertrophy after the necrosis.

The dogs with perforation of the aortic root and a sinus leading into the right heart, showed as a group slight general hypertrophy. The L/R ratios averaged about the same as those of the normals. However, the dogs that had had the lesion, even with a small sinus,

for more than 100 days showed distinct tendency toward right ventricular preponderance.

Thyroid feeding was carried out in two dogs and four thyroidectomized dogs were operated upon and aortic regurgitation produced. There were no striking changes. The data are, however, so meager that they justify no conclusions and deserve no consideration at this time.

SUMMARY OF GENERAL OBSERVATIONS IN EXPERIMENTAL AORTIC REGURGITATION

The miscellaneous data and graphic records will be reported in detail in subsequent papers. It is, however, worth while to call attention to some of the more interesting findings that have been brought out by an analysis of the information at hand. Most of the conclusions require further experimental verification. The agreement with clinical experience or other experimental results is the justification for their presentation in most instances.

MURMURS

It was most unusual to have a pure aortic diastolic murmur as the only auscultatory sign of the aortic regurgitation. A basal systolic was the most common accompaniment of the aortic diastolic murmur. A systolic murmur at the apex was likewise an almost constant finding. The aortic diastolic murmur was always better heard in the secondary aortic area in the third interspace at the left of the sternum and was well transmitted toward the apex. A striking feature was the unusually large proportion of rumbling apical diastolic murmurs and accompanying thrills that were encountered in this series. This may well be due to the fact that the lesion usually involves the posterior cusp, which is anatomically in the closest possible relation to the mitral valve, the anterior flap of which takes origin from the root of the aorta at the base of the posterior aortic sinus. The regurgitant blood stream passing the damaged posterior cusp would tend to carry the anterior mitral flap upwards and produce a functional obstruction in the mitral orifice. The Austin Flint murmur and the diastolic thrill in human cases of aortic regurgitation may be due to a similar predominant localization of the lesion. I have seen two human cases in which the greater involvement of the posterior cusp might be taken to account for the prominent signs of a functional mitral stenosis.

There was an early increase and often a later decrease in the intensity of the aortic diastolic murmur and a decrease in the prominence of the vascular signs. This might be accounted for in some instances by a gradual change in the form of the right and left anterior aortic

cusps and apparently a stretching backward in a compensatory attempt to close the gap left after the removal of the posterior cusp.

The murmurs in the dogs with perforation of the aortic root were atypical in that they were faint, heard best down the right side of the dog's thorax toward the right axilla. The transmission of the murmur toward the apex did not occur, but a transmission along the right sternal border was occasionally noticed.

THE PERIPHERAL VASCULAR SIGNS AND BLOOD PRESSURE CHANGES

The throbbing femoral, brachial and carotid vessels appeared promptly after the aortic cusp was cut. The retinal arteries also began to pulsate. The sharp systolic sound and a short diastolic murmur could sometimes be heard in the compressed femoral. A capillary pulsation was never found immediately after operation, but was elicited in a number of dogs some time later. Blood pressure curves were frequently made and the pulse pressure was found to be a fairly reliable index of the extent of the aortic lesion. Elevated systolic and lowered diastolic pressures were regularly recorded. The pressures in the femoral were found to be higher than those in the carotid artery. This is in keeping with the findings of Hill and Rowlands[28] in aortic regurgitation.

THE ELECTROCARDIOGRAPHIC AND X-RAY FINDINGS

In only one instance were electrocardiograms obtained (Fig. 5) which showed any tendency toward significant changes. This was in the case of the dog that presented the heart with the maximum local and general hypertrophy. The other 74 dogs have shown no abnormal curves. As a typical example the curves of dog No. 59 which had a free aortic regurgitation for five hundred thirty days, are reproduced (Fig. 6). These findings are in keeping with those of our human studies in which we concluded that slight and moderate unilateral cardiac hypertrophies are not faithfully recorded by electrocardiographic means. Sharp T-wave inversions and slight conduction disturbances were noted after the ether anesthesia, and when morphine was used vagus arrhythmias and conduction changes were as a rule conspicuous.

The x-ray pictures showed no enlargement immediately after operation, as one might expect from acute compensatory dilatation. In fact, in some few instances there actually appeared to be a decrease in size. In the later stages the cardiac shadows were usually distinctly increased in area.

THE ENDOCARDITIS

In the series of two hundred normal dogs' hearts that were studied, I did not find a single instance that even suggested an old endocar-

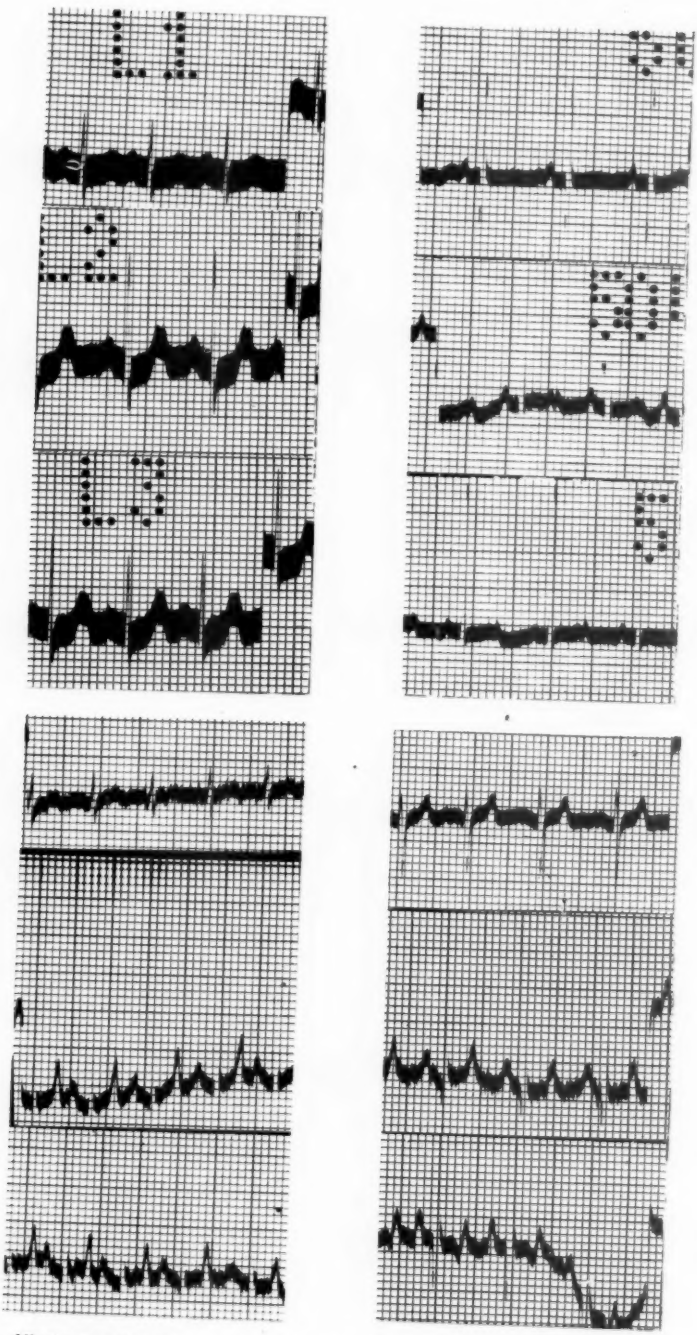

Fig. 5.—Electrocardiograms of dog No. 129, the heart of which showed the greatest relative left ventricular hypertrophy. The curves mounted on the left above are marked with the lead number L 1, L 2 and L 3, which order of lead is preserved throughout; these curves were taken 9/9/24; those on the right above were taken 11/25/24; those on the left below on 1/15/25; those on the right below on 1/27/25. The last curves were the only conspicuous abnormal ones recorded in the whole series of 150 operated dogs. The downwardly directed lead I is probably due to the fact that dogs with curves of the concordant type (Lewis) show such a curve in left ventricular preponderance just as they do when the left ventricular effects are preponderant in right bundle-branch block.

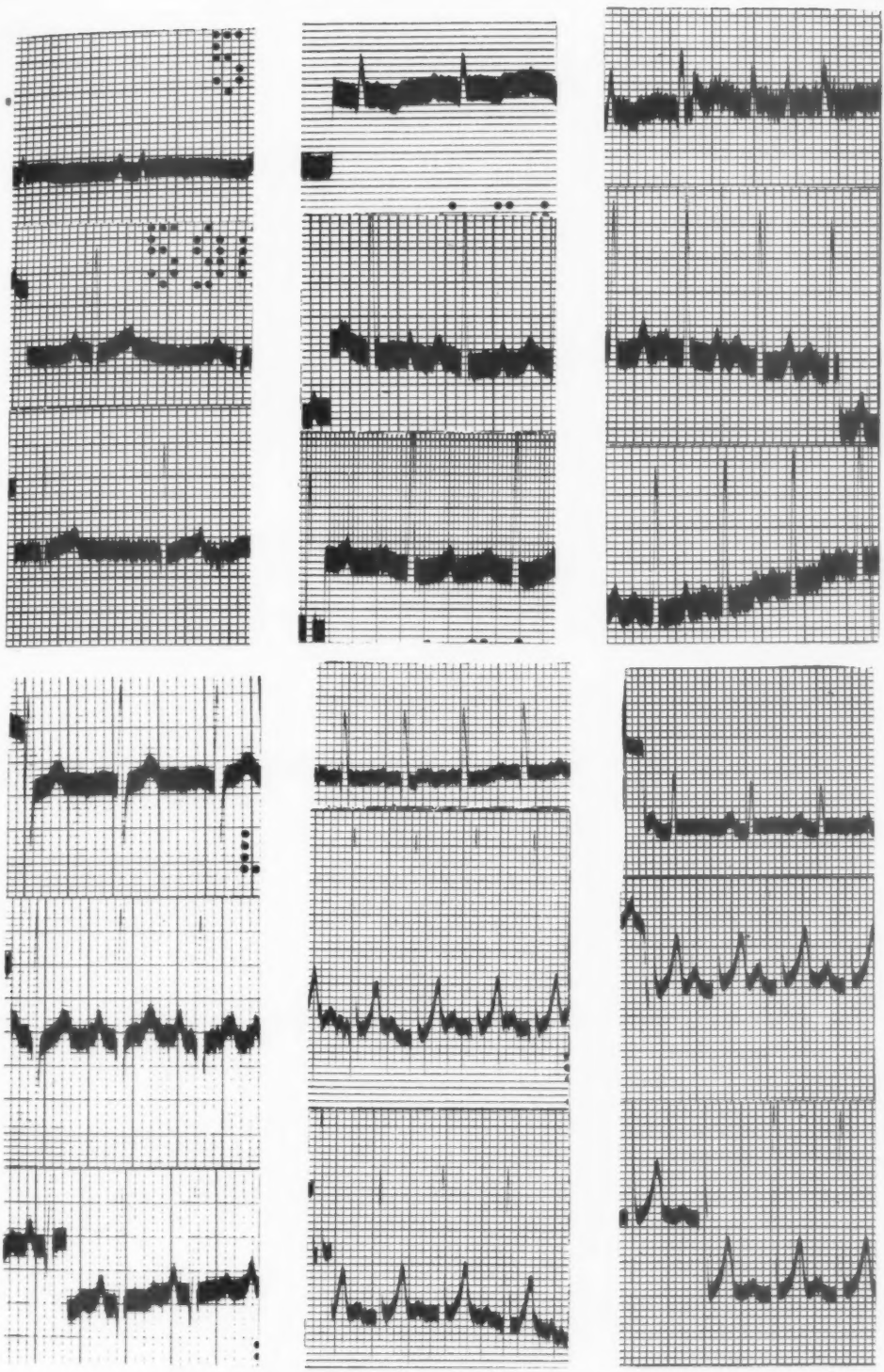

Fig. 6.—Electrocardiograms of dog No. 59, sacrificed 530 days after operation. The curves mounted above from left to right were taken on 8/19/23; 11/28/23; and 5/10/24 respectively; those mounted below from left to right were taken on 8/10/24; 11/20/24; and 1/16/25 respectively. There were no significant changes in the curve.

ditis. From this, one can conclude that the dog's heart valves are relatively immune to infection. In the early part of this experimental study, when the housing conditions for the dogs were poor, damp and with little or no sunlight, a relatively large proportion of the pups with aortic regurgitation succumbed to a spontaneous streptococcic endocarditis. Later, with better kennel facilities, the parturient bitches seemed to be most susceptible to spontaneous endocarditis. Altogether, spontaneous endocarditis developed in six pups, in two parturient bitches, and appeared healed in two bitches that had had litters of puppies, in two bitches that had no puppies and in two adult male dogs, that is 14, or 20 per cent of the dogs with experimental aortic regurgitation.

Dogs with normal valves have been found insusceptible to endocarditis even after repeated injections of cultures of streptococci from human cases. However, dogs with damaged valves were found to be uniformly susceptible to valvular implantations of streptococci injected intravenously. These observations on the experimental production of endocarditis agree with those of Connell and Corley,[29] Kinsella and Sherbourne.[30]

CHIEF CONCLUSIONS

1. Moderate degrees of cardiac hypertrophy can usually be induced in dogs by experimental aortic insufficiency. The left ventricle is the seat of the greatest relative and absolute hypertrophy. Occasionally older adult dogs are refractory to hypertrophy from pure traumatic lesions. Young dogs are much more prone to show cardiac hypertrophy.

2. The minimum time interval for the appearance of definite hypertrophy seems to be about 18 days and the maximum grade is reached in about 110 days. The extent of the hypertrophy is by no means directly proportional to the duration of the lesion. There is, however, some relationship.

3. The more important contributing factors in the degree of hypertrophy produced are (a) the youth of the dog, and (b) the presence of intracardial infection. The extent of the lesion and the activity of the dog are factors for which we have not as yet sufficient supporting evidence. The sex and breed of the dog may play a minor rôle in the degree of hypertrophy.

4. Toxic substances such as spartein sulphate and adrenalin, tend to decrease the degree of hypertrophy.

5. The murmurs are similar to those obtained in aortic regurgitation in man. The frequency of the occurrence of the Austin Flint rumble at the apex and the diastolic thrill suggest that these phenomena depend in a large measure upon the involvement of the pos-

terior aortic cusp. A tendency to compensatory change was noted in some valve leaflets.

6. The peripheral vascular signs, except the capillary pulse, appeared promptly and persisted. Capillary pulsation was often elicited later.

7. The electrocardiograms in all but one instance failed to show the signs that suggest preponderant left ventricular hypertrophy.

8. Spontaneous endocarditis appeared in 20 per cent of the experimental aortic regurgitation dogs. Pups, especially with poor hygienic surroundings, and parturient bitches were most susceptible to infection.

9. The solution of the problem of cardiac hypertrophy is still out of our reach. The above results, however, seem to indicate that not one but a number of factors are active. Further investigations along these lines may eventually lead to a clearer conception of the genesis of cardiac hypertrophy.

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Department of Reviews and Abstracts

Collective Review

THE CARDIAC NERVES IN ANGINA PECTORIS*

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THE aorta and coronary vessels are surrounded by nerve fibers forming plexus in which minute sympathetic ganglia are located. These aortic and coronary plexus contain sympathetic nerve fibers, derived from the ganglia of the cervical and upper thoracic portions of the sympathetic trunk by way of the superior, middle, and inferior cardiac sympathetic nerves, and also fibers derived from the vagus through its cardiac branches. It is the purpose of this paper to present what is known concerning the rôle which these extrinsic nerves play in angina pectoris.

It must be admitted that it is not possible on the basis of the known facts of anatomy and physiology, to explain the beneficial results of cervical sympathectomy in angina pectoris. In fact, medical authorities are not agreed as to the nature of this disease, if, indeed, it should be regarded as a disease rather than a syndrome appearing in a number of abnormal cardiovascular conditions. Whether or not the intense pain which characterizes the anginal attacks is due to stretching of a diseased aorta, to spasm of the coronary arteries, or to anemia of the myocardium, the pain in itself clearly indicates that there is an irritation of sensory fibers in the heart wall or in the immediately associated arteries.

The course of the sensory fibers for the heart and associated arteries is well known and is illustrated in the accompanying figure. From the cardiac plexus, which supplies the aorta, coronary vessels, and heart, afferent impulses are carried to the brain along the vagus nerve and to the spinal cord along the cardiac branches of the middle and inferior cervical sympathetic ganglia, the sympathetic trunk, white rami, and upper three or four thoracic nerves. The chief pain in angina pectoris is referred to the chest wall and the inner side of the left arm in the area of cutaneous distribution of the first three or four thoracic nerves. Since, as demonstrated by Head[1] in 1893,

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pain in visceral disease is referred to the areas of cutaneous distribution of those segmental nerves from which the viscus in question receives its afferent innervation, it is evident that the pain in question is mediated through these upper thoracic nerves and the corresponding white rami. In some cases there is pain and tenderness in the head and neck. This, Head attributes to afferent impulses which reach the brain along the vagus nerve and cause referred pain in the areas of cutaneous distribution of the trigeminal and the third and fourth cervical nerves. In an interesting case of syphilitic aortitis reported by Penfield[2] these pains in the upper part of the neck and head persisted after removal of the middle and inferior cervical and first thoracic sympathetic ganglia on both sides. This can best be explained, in line with Head's work, as a reference from the vagus.

Histologically, it is possible to trace sensory fibers through the sympathetic system because of their relatively large size. Edgeworth[3] has traced large sensory fibers to the cardiac plexus in the dog from the vagus nerve and from the white rami of the upper three thoracic nerves. Those from the white rami reached the cardiac plexus after passing through the stellate ganglion, the annulus of Vieussens, the middle and inferior cervical ganglia, and the nerves passing from these ganglia to the heart. By the study of serial sections of the sympathetic trunk in the cat we have been able to confirm Edgeworth's findings.[4] No large sensory fibers were found in the cervical sympathetic trunk going to the superior ganglion, The nerves removed from patients suffering with angina usually show, on histologic examination, no large sensory fibers in either the cervical sympathetic trunk or the superior cardiac nerve which descends from the superior cervical ganglion to the cardiac plexus. In one case, however, a few were found in both of these nerves; but it is possible that they may have come from the vagus through the branches of communication between the nodose and superior cervical sympathetic ganglia. There is no good reason for assuming that the sensory pathways for the heart in man are essentially different from those in the cat and dog. The course of the sensory fibers from the heart as determined by histologic studies is shown in the diagram. The arrows indicate the direction of conduction and the dotted line a possible but highly improbable pathway.

This conception of the sensory pathways is supported by physiological evidence. Langley,[5] working with cats, cut the sympathetic trunk below the fifth thoracic white ramus and, at the same time, the cardiac sympathetic nerves. When these nerves were stimulated proximal to the cut, reflex movements were obtained which ceased when the upper five thoracic white rami were divided. If connections between the vagus and superior cervical sympathetic ganglion had been divided, Langley never obtained reflex movements of the body from stimulating this ganglion

or the upper part of the cervical sympathetic trunk. Nor were reflexes obtained from the vertebral nerve after it had been carefully separated from a branch of the seventh cervical nerve which accompanies it. These experiments show that in the cat the upper portion of the cervical sympathetic trunk contains no sensory fibers and that the pain fibers for the heart run through the lower cervical and upper thoracic portion of the sympathetic trunk and the upper white rami to the upper thoracic spinal nerves.

Eppinger and Hofer[6] obtained good results in cases of angina pectoris by section of a branch of the vagus which they called the depressor nerve. This is a well defined nerve in the rabbit. It carries sensory fibers from the arch of the aorta, and when it is stimulated there results a reflex fall in blood pressure. It is doubtful if this nerve has a separate existence in man, its fibers probably being incorporated in the main trunk of the vagus. The uncertainty as to the existence and topography of this nerve is evident from the directions given for its identification. The vagus is exposed up to the point where it enters the jugular foramen. Each of the branches from the upper part of the vagus is then dissected for some distance. Only those fibers which run free into the thorax or those which after separation from the vagus or superior laryngeal nerves join the vagus again are considered as belonging to the depressor nerve. Surely these are not sufficient grounds for identification. This would require that a fall in blood pressure should be obtained by stimulating the twig thought to be the depressor. Eppinger and Hofer out of consideration for their patients failed to make the test in any of their five cases. Odermatt[7] stimulated the nerve which he thought was the depressor without producing any change in the blood pressure or the pulse. It is evident, therefore, that the nerve which he cut was not the depressor and yet there was no recurrence of anginal attacks during the fourteen days that the patient survived the operation.

Jonnesco and Ionescu[8] recently obtained a slight drop in blood pressure from stimulating a descending branch of the superior laryngeal nerve; but they also obtained a similar reflex from cardiac branches of the sympathetic, and the identification of this twig as the depressor nerve remains doubtful.

Wenckebach[9] in his most recent communication on the subject says that the absence of a clearly differentiated depressor nerve in so many cases was a great disappointment. He now believes that section of this nerve will not become the operation of choice in angina pectoris, in view of the fact that it is often difficult or even impossible to find.

Recently Jonnesco and Ionescu[8] made some very interesting and important observations on the sensory nerves to the heart in the course of operations on the cervical portion of the sympathetic trunk, carried out under cervical anesthesia with 0.04 gm. stovain. For purposes of

control some operations were performed under chloroform anesthesia and others after the local injection of novocaine. The blood pressure was registered directly from the radial artery with a mercury manometer. In some patients they obtained, on stimulation of the cephalic end of the sympathetic trunk, a slight pressor effect, which, however, disappeared after destruction of all connections between the superior cervical sympathetic ganglion and the vagus. In many cases stimulations of the cephalic end of the sympathetic trunk produced no effect, and in these cases they found no connections between this part of the sympathetic and the vagus nerve. In one case stimulation of the central cut end of a cardiac nerve from the inferior cervical sympathetic ganglion gave motor and respiratory reflexes, and the patient complained of pain in the ventral wall of the thorax. In another case stimulation of a cardiac branch given off from the sympathetic trunk immediately above the inferior cervical ganglion gave respiratory reflexes and pain referred to the axilla. In still another case at the time that the stellate ganglion was being removed the patient complained of severe pain in the left arm.

In a patient with angina pectoris, Schittenhelm and Kappis[10] injected novocaine into the upper part of the sympathetic trunk without effect, but injection of the lower part caused the pain to disappear. Injection of the vagus did not relieve the pain.

One of Leriche's[11] patients had an anginal attack during the operation before the stellate ganglion had been laid bare. As a result of the infiltration of the inferior cervical ganglion with novocaine the pain ceased at once.

These surgical observations confirm the conclusions drawn from the location of the referred pain and show that in man, as in the cat, pain in the heart and aortic arch is mediated by way of the middle and inferior cardiac nerves through the lower cervical and upper thoracic portions of the sympathetic trunk and thence along the upper thoracic white rami and the corresponding spinal nerves of the left side to the spinal cord.

Following a suggestion made by François Frank, Jonnesco[12] in 1916 removed the middle and inferior cervical and the first thoracic sympathetic ganglia on the left side in a severe case of angina pectoris in order to interrupt the path for painful sensory impulses from the heart. The patient, who was kept under observation for four years, remained free from anginal attacks. Successful results in angina from essentially similar operations were reported in 1923 by Brüning, Pleth, Kümmell and Kappis.

That this operation should stop anginal pain can readily be understood from what has been said about the course of the sensory fibers from the heart, but the work of Coffey and Brown[13] seems to make this simple explanation untenable. These authors found that the same

results can be obtained by sectioning the sympathetic trunk and superior cardiac nerve below the superior cervical ganglion or by excising this ganglion. At first they were inclined to believe that this demonstrated that the painful afferent impulses from the heart reached the brain through some of the connections of the superior cervical ganglion. A possible but highly improbable path for such impulses is indicated by the dotted lines in Fig. 1. Histological, physiological and clinical evidence makes it almost certain that in high cervical sympathectomy, as practiced by Coffey and Brown, the afferent fibers from the heart are not damaged.

At present no satisfactory explanation can be given of the beneficial effect of cervical sympathectomy in cases of angina pectoris and none is likely to be forthcoming until we know more about the pathology of the disease and about the innervation of the heart and associated vessels. The good results which have been obtained by removal of the left superior cervical sympathetic ganglion or by simply cutting the sympathetic trunk and superior cardiac nerve beneath this ganglion suggests the following hypothesis: Vasoconstrictor fibers for the coronary vessels and arch of the aorta reach the cardiac plexus from the left superior cervical sympathetic ganglion by way of the superior cardiac nerve. The anginal attacks are due to arterial spasm. The removal of this ganglion or the section of the sympathetic trunk and superior cardiac nerve below the ganglion gives relief by interrupting the vasoconstrictor path and thus preventing spasmodic contraction of the coronary vessels or arch of the aorta. In the rare cases of dextral radiation of the anginal pain relieved by removal of the right superior cervical ganglion (Coffey and Brown) it is necessary to assume that this ganglion is the chief source of the vasoconstrictor fibers. While this hypothesis seems the most satisfactory (Holmes and Ranson, Coffey and Brown, Jonnesco) it cannot be regarded as anything more than an hypothesis until the vasoconstrictor fibers which it postulates have been demonstrated physiologically.

Physiologists are in doubt as to whether or not the coronary vessels receive vasoconstrictor fibers. According to Bayliss[14] there is no evidence that they do. Wiggers[15] has shown that there is some evidence of the existence of a vasomotor supply for these vessels. Stimulation of the vagus nerve in the atropinized dog decreases the outflow from the cardiac veins in the absence of any change in the contraction of the auricles and ventricles or in general blood pressure. This would seem to indicate that the coronary arteries receive vasoconstrictor fibers from the vagus. But, on the other hand, adrenalin, when perfused through the quiescent heart, diminishes the coronary outflow, and this indicates that the coronary arteries receive vasoconstrictor fibers from the sympathetic. The results which have been obtained on mammals are therefore contradictory.

But the recent careful work of Drury, Smith and Sumbal[16] on the coronary vessels of the tortoise clearly show that these vessels are under the influence of vasodilator fibers derived from the vagus and vasoconstrictor fibers derived from the sympathetic system. It remains, however, to be shown that the coronary vessels of man have a similar innervation.

In spite of the lack of any definite information concerning the vasomotor innervation of the coronary vessels it seems probable that high

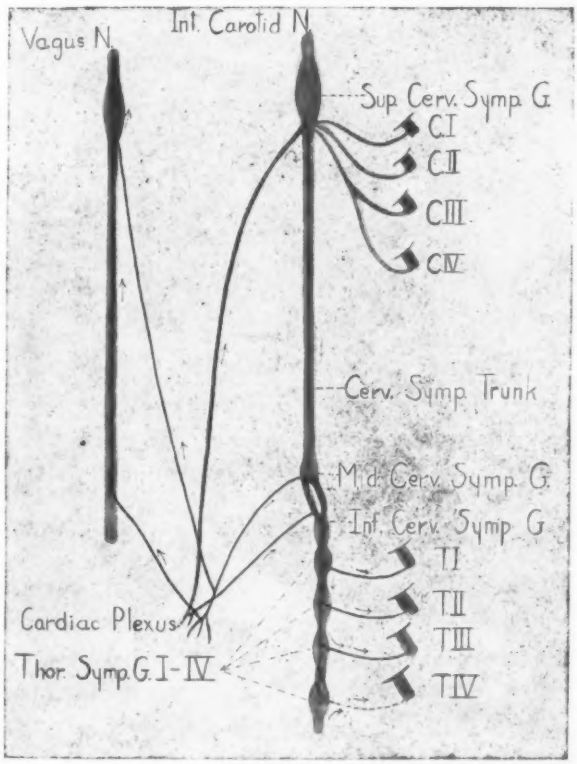

Fig. 1.

cervical sympathectomy as practiced by Coffey and Brown produces its good results by interrupting the vasoconstrictor path and thus preventing reflex spasm of the coronary vessels. At any rate it is clear that in the more successful cases which have been reported the sense of constriction, the fear, the physical prostration and other features of the attacks were relieved quite as much as the pain. From being bedridden because of the anginal attacks brought on both by effort and emotion the patients are returned to active life and are able to follow occupations requiring considerable effort. The operation seems to accomplish more than the mere relief of pain. While, of course, sym-

pathectomy can have no effect upon lesions already existing in the heart and associated vessels it is possible that by preventing reflex constriction of the coronary vessels it may lead to a better circulation and improved nutrition of the cardiac muscle. These are the conclusions to which Jonnesco and Ionescu[18] have come as a result of their ten years' experience with sympathectomy for the relief of cardiac pain.

Why are these beneficial results obtained from a unilateral operation and why does removal of only the superior cervical sympathetic ganglion on the left side suffice in most cases to prevent recurrence of the anginal attacks? The superior cardiac nerve which leads from this ganglion to the heart is not present in animals and consequently is not subject to direct experimental investigation. In the human we know that it takes part in the formation of the cardiac plexus, but in the adult this plexus is so intricate as to defy analysis.

The embryologic picture, however, gives us a clue. In the human embryo the superior cardiac nerve goes to the bulbar plexus which surrounds the bulbus cordis and its derivatives, the aorta and pulmonary artery, while the middle and inferior cardiac nerves go to the atrial plexus. The atrial plexus, since it supplies the region in which the heart beat originates, may be assumed to receive the sympathetic cardio-accelerator fibers. The bulbar plexus is situated near the beginning of the aorta. From it arise offshoots forming plexus on the coronary arteries. These offshoots may be assumed to receive vasoconstrictor fibers which probably come through the superior cardiac nerve. Since the aorta is formed from the left side of the divided bulbus cordis it might be assumed that the vasoconstrictor fibers for it come from the left superior cardiac nerve. If future investigation should prove that this assumption is correct it would be possible to explain the effects of high left cervical sympathectomy as the result of the interruption of the vasoconstrictor path to the aorta and coronary vessels.

Excellent results have followed the high cervical sympathectomy as practiced by Coffey and Brown, as well as the more extensive operation of Jonnesco, and only an accumulation of clinical experience can make clear which should be the operation of choice. In the meantime there are certain considerations which should influence the decision. High cervical sympathectomy is a simpler operation with lower mortality (Jonnesco and Ionescu) and has the advantage that the sensory and accelerator fibers for the heart are not divided. If, as suggested by Holmes and Ransom[17] and now accepted by Jonnesco[18] and Coffey and Brown,[13] the beneficial results of high cervical sympathectomy are due to interruption of the vasoconstrictor pathway to the heart and the prevention of reflex spasm of the coronary vessels, this operation should be the operation of choice whenever there is little evidence of organic cardiac or aortic disease. When, however, there is reason to believe that the pain is due to organic disease, as in cases of aortitis, better and more

permanent results may be expected if the sensory fibers are severed by the Jonnesco operation.

Recent studies of Jonnesco[18] would indicate that the function of the heart is little if at all impaired by his operation. Observations on the pulse and blood pressure made before and after the operation show that the variations after the operation are no greater than those seen in the same patients before the operation. He has never seen disturbances of cardiac rhythm. Roentgenological tests show that the form and dimensions of the heart are not changed. Adrenalin acts on the heart just as well after double sympathectomy as before. Functional tests of the heart have given good results both in convalescents and in patients operated upon years before.

In conclusion it may be said that in carefully selected cases of angina pectoris left cervical sympathectomy has given good results; the pain has been stopped, and many of the patients have been returned to active life. It seems probable that these beneficial results are due in the case of high cervical sympathectomy purely to an interruption of the efferent limbs of the reflex arcs involved in initiating the attacks. In the more complete operation of Jonnesco the same thing is accomplished and in addition the path for painful afferent impulses from the heart is also interrupted.

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Selected Abstracts

Middleton, William S.: The Positive Venous Pulse: New Method for its Detection. Am. Jour. Med. Sci., 1926, clxxi, 341.

The author reports a case of cardiac failure due to myocarditis in which a positive centrifugal jugular pulse was noted. The venous pressure was found to be 24 to 26 cm. of water. When the hand was elevated to a level of 26.5 cm. above the midaxillary line, a positive centrifugal pulse appeared in the veins on the dorsum of the hand. He suggests this as a procedure for recording the venous pressure. With the patient recumbent or sitting the arm can be elevated slowly until there is collapse of veins and a positive venous pulse appears in the veins of the forearm. The distance in centimeters from the arm to the level of the right auricle corresponds to the venous pressure. The level of the auricle in the recumbent position may be taken on the midaxillary line; in the sitting position the level is at the xiphosternal notch. He suggests the radial vein as a point of observation.

He discusses the various ideas which exist in regard to the value of a positive venous pulse as a sign of tricuspid insufficiency and cardiac failure.

Kanner, Leo: The Influence of Rest, Sleep, and Work upon the Action of the Heart. Am. Jour. Med. Sci., 1926, clxxi, 331.

The author studied patients with healthy hearts, with valvular disease, and with varying pulse rates by means of clinical examination, in combination with electrocardiographic and cardiophonographic records. He estimates the time of contraction of the heart to be 33.5 to 37.5 per cent of the total time. He designates this working period of the heart as the "time of action." He studied this phenomenon under varying conditions of sleep, rest, and work. He found that with increased pulse rate after work or stimulation there is an increased "time of action" in the heart. He also found that the duration of the conduction of the electrical stimulation through the bundle of His, is absolutely prolonged during rest and absolutely shortened during and immediately after work.

Observations on these same subjects in periods of quiet and actual sleep showed that the changes were of such slight degree as to have little significance.

Klotz, Oskar: Arteriosclerosis. Canadian Med. Assn. Jour., 1926, xvi, 11.

This address outlines the most recent conceptions of arteriosclerosis, embodying ideas which have been emphasized by the author in other communications.

He calls attention to the fact that there may be a variety of pathological changes in the arterial wall, which in the end result in a thickening of the vessel and a hardening of its structure; and that these lesions may be merely stages in the arteriosclerotic process. He emphasizes as etiological factors three important conditions: (1) the influence of bacterial agents in causing damage in the nature of inflammation of the arterial wall; (2) the influence of the virus of rheumatic fever upon the arterial system, and (3) the influence of work in causing thickening of peripheral vessels, particularly in the lower extremities from continued high arterial pressure.

He says that it is quite common to find a localization of the bacteria of several diseases upon the outer walls of the arteries and an invasion of the middle coats by these organisms. The usual location is about the aorta and its branches, they

being found less commonly in the peripheral vessels. The process consists of an inflammatory reaction about the infection leading to a focal destruction of the intrinsic tissues of the arterial wall. This, then, is followed by the development of scar tissue. The character of the lesion varies in degree, being often so small as to escape detection, while others develop a superficial thickening and a nodular protrusion of the intima into the lumen of the vessel.

The lesions which occur in rheumatic fever are similar to those described by Aschoff. The lesions, as in the heart, may be few and scattered or may be disseminated widely and involve the walls of the vessels very severely. They are located commonly in the aorta but also in the peripheral vessels of the brain, kidney and extremities. The immediate effect on the arterial wall may not be great but the scarring which results from the chronic inflammatory process is prone to become cumulative. Eventually, in advancing years, arteriosclerosis develops more and more, and there results a definite influence upon the circulation.

The type of arteriosclerosis best known to the clinician involves the peripheral palpable arteries of the extremities, with or without involvement of the aorta and central vital organs. In this type the outer and inner coats of the arteries are unaffected while the middle coat is in a state of degeneration, with destruction of its muscular elements and a replacement of them by calcified material. These peripheral scleroses, which are so common, appear to bear the direct relation to the activity of the tissues which they supply.

He points out that the relationship between high blood pressure and arteriosclerosis is still not clear. It is true that the two conditions frequently go hand in hand, but it is equally true that the gradations are by no means parallel. He calls attention further to various relationships between the two conditions, especially that hypertension by itself can hardly cause nodular thickening of the intima such as is commonly found in the vascular scleroses.

Olmsted, Harry C.: Intradermal Salt Solution Test in Cardiac Disease in Children. Arch. Int. Med., 1926, xxxvii, 281.

Using the technic of McClure and Aldrich, the author tested 42 cardiac children with intracutaneous injections of 0.8 per cent solution of sodium chloride. The time of disappearance of the wheal was noted. Those cases with an edema showed a decreased disappearance time, probably the result of an increased water affinity of the adjacent tissues. This phenomenon was limited to the edematous regions of the body. There seemed no relationship between the toxic state of the patient and the state of circulation before edema appeared. The test proves of limited value in their hands.

Kern, Richard A.: Paroxysmal Tachycardia Following the Use of Air in Testing Fallopian Tube Patency. Jour. Am. Med. Assn., 1926, lxxxvi, 623.

The author reports a middle-aged woman who had air injected into the peritoneal cavity through the fallopian tube. Several hours later, in the upright position, she experienced distress and pain in the left chest. She was found to have a pulse rate of 152 with regular, normal rhythm. No other abnormal heart signs were present. When placed in the recumbent position the pain was relieved and the pulse rate was halved to 76. No electrocardiogram was made.

Geraudel, E.: The Adam-Stokes Syndrome and Its Pathogenesis. Bull. de l'Acad. de Med., 1925, xciv, 1297.

Geraudel believes that the cause of the Adam-Stokes syndrome is to be sought in the vessels supplying the conduction system rather than in the conduction system itself. He reports a typical case of the paroxysmal form in a diabetic, aged fifty-

six years. In the last two months of his life, this patient suffered from syncopal attacks, during which the pulse fell to 30 and sometimes to a point as low as 18. During the intervals between seizures, the pulse was 66. Death occurred during a syncopal attack. Careful examination by serial sections of the A-V node and the bundle of His and its branches revealed no changes. There was, however, stenosis of the artery supplying this part of the conduction system, and this explains the disturbed ventricular rhythm. The artery to the sinoauricular node was unchanged. Death was apparently due to a prolonged spasm shutting off the blood from the conduction apparatus and consecutive arrest of the ventricular contraction. If the impaired circulation is due to a permanent lesion, treatment will be without effect. If, on the other hand, the disturbed rhythm is due to spasmodic vasomotor changes, it may be possible to influence these.

Keefer, Chester S., and Resnik, William, H.: Paroxysmal Dyspnea as a Symptom of Syphilitic Aortitis. Arch. Int. Med., 1926, xxxvii, 264.

From a study of 82 cases of syphilitic aortitis confirmed by autopsy the authors conclude that paroxysmal dyspnea was present only as a symptom of aortic insufficiency, hypertension, or aneurysm of the root or arch of the aorta. They conclude that it may be an important symptom in the differentiation between aortic insufficiency of syphilitic and of rheumatic origin.

Lutembacher, R.: The Disturbance of Cardiac Rhythm in Experimental Diphtheria. Ann. de Med., 1925, xviii, 278.

Lutembacher injected rabbits intravenously with diphtheria toxin and studied the changes in the heart rhythm. Sinus bradycardia occurred early (second to fourth day), but was later followed by acceleration and the appearance of auricular, nodal, and ventricular extrasystoles, crises of paroxysmal tachycardia, and disturbances of conduction in the His bundle and its branches (prolongation of P-R interval, heart-block). Microscopic examination showed myocardial lesions in each case. The early bradycardia is believed to be of vagal origin, but the later disturbances of rhythm seem clearly to be due to a direct action of the toxin on the myocardium and the conduction system.

Field, H., Jr., and Bock, A. V.: Orthopnea and the Effect of Posture upon the Rate of Blood Flow. Jour. Clin. Invest., 1925, ii, 67.

These authors have studied the rate of blood flow on normal subjects of ordinary type in recumbent, sitting, and standing positions. The average rate of blood flow while sitting was 76 per cent, and while standing it was 50 per cent of the rate while reclining. Inasmuch as the pulse rate increased from an average of 63 per minute in the reclining position to 65 per minute in the sitting position and 90 per minute in the standing position, the output per minute was tremendously diminished in the upright posture. This is also indicated by the blood pressure findings. After the subject had been standing for a time the pulse pressures were gradually diminished, often to 5 or 10 mm. of mercury, and sometimes auscultatory vascular sounds were almost inaudible.

In discussing these findings the authors attempt to explain the reason for the upright positions assumed by cardiac patients with dyspnea and muscle failure. They state that the diminished output of the heart which occurs in the upright position is admirably adapted to reducing the congestion in the lungs. It increases the vital capacity and makes breathing more comfortable. It should give relief in much the same way as does venesection. Instead of the total volume of blood being reduced, a part of it stagnates in the dependent parts; a smaller amount is returned to the heart; the output of the right heart is diminished; this smaller

amount of blood should be more readily dealt with by the left heart and pumped on through the systemic circulation and the congestion in the lungs should be relieved.

Bussiere, Henry C., and Rhea, Lawrence, J.: Acute Rheumatic Fever and Chorea in Children. Canadian Med. Assn. Jour., 1926, xvi, 35.

The authors have analyzed the various clinical features of 100 children in the Memorial Hospital, Montreal, who were suffering from acute rheumatic fever and chorea. The results of their analysis are in accord with impressions which prevail in other sections of this continent and present nothing new. They call attention to the frequency with which chorea and rheumatic fever are related in the same child.

Dresbach, Melvin, and Waddell, Kenneth, C.: K-Strophanthidin Emesis in Cats with Denervated Hearts. The Seat of Its Action. Jour. Pharm. and Exper. Therap., 1926, xxvii, 9.

The authors studied the effect of strophanthidin introduced by various paths into cats who had been previously operated upon so as to isolate the heart from all nervous control. They conclude from their experiment that strophanthidin will induce vomiting after thorough denervation, provided the cat has been given time to recover from the immediate effects of operation. They conclude that the action of the drug is central in its location and state that the vomiting center in the medulla is the probable location. In preparing cats for the experimental study the authors have found numerous paths of nerve control to the heart other than the vagi and the paths through the stellate ganglion. These paths, as well as the procedure for severing them, are described in detail.

Danielopolu, D.: The Surgical Treatment of Angina Pectoris. Brit. Med. Jour., 1926, i, p. 80.

The author reviews the development of his ideas concerning the proper operation for the relief of angina. He states that his present attitude is to recommend the removal of all paths of the cardioaortic sensory fibers without touching the important cardiac accelerator fibers which pass through the stellate ganglia. These sensory cardiac paths include the cervical sympathetic trunk, the fibers of the cervical vagus nerve and its intrathoracic branches, the vertebral nerve and communicating branches uniting the inferior cervical ganglion and the first thoracic nerve with the sixth, seventh, and eighth cervical and first dorsal nerves. He feels that unfavorable results come from removal of or interference with the stellate ganglia.

McCrudden, Francis H.: Sinus Respiratory Arrhythmia in Children with Rheumatic Heart Disease. Jour. Am. Med. Assn., 1926, lxxxvi, 535.

The author analyzes his findings in a small, unselected group of 100 children, all of whom showed rheumatic heart disease with valvular injury severe enough to be in bed. Eighty of the 100 cases showed sinus arrhythmia so evident as to be easily detected. The cases with arrhythmia showed a lesser degree of enlargement, a lower percentage of activity, fewer cases with pulse rate over 100, fewer signs of decompensation, and fewer signs of more than simple myocardial damage. In other words, in the 20 cases not showing arrhythmia, these phenomena were all present in greater degree and frequency. He also notes the subsequent course of the two groups. Those children with the arrhythmia died in a short time after the original observation. While the absence of sinus arrhythmia in children does not distinguish those having heart disease from those not having it, it is evident that it indicates a bad prognosis.

Thatcher, Catherine, and White, Paul D.: The Electrocardiogram in Myxedema. Am. Jour. Med. Sci., 1926, clxxi, 61.

Fourteen cases of myxedema have been studied with a string galvanometer at the Massachusetts General Hospital. Basal metabolic rates were also determined during the same period. In the electrocardiograms in every case there was a decrease in the height of the T-wave in Lead II below normal, the highest reading being +1 ml., whereas the T-wave in Lead II should normally have an upright deflection of 2 ml. or more. There were no other abnormalities. The QRS complex in some instances was decreased in amplitude, approaching the "low potential" type and increasing as did the T-wave with thyroid treatment. This low potential type is similar to that seen in myocardial exhaustion due to serious coronary sclerosis.

This fact is evidence that the heart action is sluggish during myxedema, in accord with the recent finding of Einthoven that the electric and mechanical expressions of muscular activity are not only synchronous but also tend to be parallel in degree.

Resnik, William H.: Observations on the Effect on Anoxemia on the Heart. Jour. Clin. Invest., 1925, ii, 93.

I. *Auriculoventricular Conduction.*—Using dogs under experimental conditions the author has studied the effect of varying degrees of anoxemia in the heart when the auricle is stimulated by induced currents at varying rates. He finds that anoxemia produces first, a decrease, and later, an increase of P-R interval, the latter being favored by severe anoxemia of long duration, by a rapid cardiac rate, and by deterioration of the general condition of the animal from one cause or another. He states that the cause of impairment of auriculoventricular conduction in the later stages of anoxemia is due to a direct influence in the heart muscle, produced by oxygen lack, whatever may be the fundamental mechanism by which such a lack of oxygen exerts its effect. The cause of the initial quickening of auriculoventricular conduction is not clear. As a result of his experiments he states that vagal influence may be dismissed as a factor. One must, however, consider the possibility of stimulation of the sympathetic nerves. That this cause may operate is not conclusive since evidence exists against it; e. g., the decrease of the P-R interval was not associated with those alterations of the electrocardiogram which have been described by Rothberger and Winterberg. The author suggests that the changes in conduction are due to a direct effect on the myocardium.

II. *Intraventricular Conduction.*—The changes observed are similar to those which occurred in auriculoventricular conduction except that the degree is less. It is probable that ventricular aberration in clinical cases is an indication of more or less serious disturbance of the function of Purkinje tissues. He points out that there was a definite tendency for ventricular fibrillation to develop, particularly when the anoxemia was severe and prolonged. In this study four animals were used.

III. *Changes in the Auricles with Particular Reference to the Relationship between Anoxemia and Auricular Fibrillation.*—The results which were obtained with stimulation during anoxemia indicate definitely that anoxemia predisposes the auricles to fibrillation. Apparently some other factor besides anoxemia is necessary to initiate this arrhythmia. In these observations, using the normal heart of the dog, this additional factor was the rapid stimulation of the auricles by a faradic current. Whether or not this second factor may be present in the various clinical conditions in which anoxemia seems to play a rôle in causing transient auricular fibrillation it is difficult to determine. He points out that the clinical conditions which produce anoxemia also favor the development of a circus movement in the auricle, i.e., shortening of the refractory period and lengthening of

the rate of conduction. Under these conditions something may occur in the course of clinical heart disease which produces fibrillation.

He also states that his experiments show the sinoauricular node to be highly sensitive to anoxemia in much the same way as the bundle of His.

Ashman, Richard: Conductivity in Compressed Cardiac Muscle. I. The Recovery of Conductivity Following Impulse Transmission in Compressed Auricular Muscle. Am. Jour. Physiol., 1925, lxxiv, 121.

This paper deals with the recovery of conductivity in the compressed auricular muscle of the turtle heart. The heart was atropinized, excised, rendered quiescent by removal of the sinus and so arranged that simultaneous myograms of auricle and ventricle could be recorded. By means of a heart clamp varying degrees of compression were established at the atrioventricular groove, although the compressed muscle was chiefly auricular. The auricle from which myograms were obtained was stimulated electrically and, since the heart was otherwise quiescent, the durations of the cycles were thus controlled. The duration of the A-V interval was taken as a measure of the conductivity. Since the condition of the compressed muscle remained relatively constant for only short periods, each curve of recovery was plotted from separate single series of responses, the whole series being obtained within about two minutes. The A-V intervals were plotted as ordinates against the auricular cycle lengths, varied irregularly, as abscissae. The resulting curve was taken as indicating the course of recovery of conductivity.

The most important results and conclusions were:

(1) That following the transmission of an impulse through the compressed muscle there is first an interval during which a second impulse, if discharged from the auricle, will fail to reach the ventricle. This is followed by a period during which the impulse is transmitted slowly, then more rapidly until finally the resting conductivity is regained. The course of recovery is along a smooth curve. There is no way of calibrating the compression, but in general it may be stated that the greater the compression (injury), the longer the A-V interval for the resting tissue, the longer the interval during which no impulse will be transmitted and the slower the subsequent recovery of conductivity. These periods may, in fact, be enormously prolonged. In a given heart the recovery of conductivity in all structures other than that compressed can be shown to have been completed during that interval when no impulse will be transmitted through the compressed region, provided the compression is sufficiently great. In such cases we can say with certainty that the recovery curve represents the course of recovery of conductivity in the compressed muscle alone.

(2) That a blocked impulse may influence the rapidity of conduction of a subsequent impulse. With a moderate degree of compression, an impulse arriving at the compressed region during the first half of that interval during which a second impulse is blocked will not appreciably prolong the conduction time for a subsequently transmitted impulse. But as the blocked impulse falls later and later during that interval it prolongs the conduction time of the subsequent transmitted impulse more and more, so that a blocked impulse which just fails of transmission depresses conductivity about 70 per cent as much as an actually transmitted impulse. Thus, in a clinical case of 2:1 block, the blocked impulse will influence the P-R interval following the dropped beat.

(3) Evidence suggesting that the recovery of conductivity following the blocked impulse is somewhat slower than that following the transmitted impulse is also given. This is attributed to a cumulative fatigue effect.

(4) Since there is direct evidence (Drury) that the impulse traversing compressed muscle becomes weaker and travels more and more slowly as it advances

so that it may die out at any point, it will be evident that that interval following the transmission of one impulse during which a second impulse is blocked cannot be regarded as coextensive with an absolute refractory period. It will also include the earliest part of the relative refractory period.

Anomalous results have not been lacking in these experiments. In a few hearts the variations in the A-V intervals were so slight as to come within the limits of error in measurement (myograms). In one case, no matter how the cycle lengths were varied, a 2:1 block was consistently obtained. No explanation can be offered for this phenomenon. In two or three cases, discontinuous recovery curves were obtained, suggesting that two pathways were open to the impulses.

Ashman, Richard: Conductivity in Compressed Cardiac Muscle. II. A Supernormal Phase in Conductivity in Compressed Auricular Muscle. Am. Jour. Physiol., 1925, lxxiv, 140.

This paper points out that there may be supernormal phase in conductivity. This phenomenon appeared under conditions which contributed to fatigue of the muscle, but fatigue effects may be obtained without evidence of a supernormal. The converse has not been observed. The method and experimental animals were identical with those of the first paper, excepting that some experiments were done with ventricular strips, but everything observed with the ventricular muscle has also been shown for the auricular.

In a typical experiment it was found that the recovery curves, returning rapidly to normal or resting conductivity, passed beyond this line for a greater or lesser distance and then more gradually returned to the line representing the resting conductivity. Thus an impulse arriving at the compressed region four or five seconds after the transmission of a previous impulse is actually transmitted more rapidly, and in many cases much more rapidly than one delivered after 10, 20 or 30 seconds. Consequently, with an increase in the degree of compression a stage may be reached when all impulses will be blocked excepting those falling on or near the crest of the supernormal phase.

There is considerable difficulty, under the conditions of these experiments, in determining the exact form of the supernormal recovery curve. This is due to two phenomena. The first is the appearance, after rest, of a treppe in conductivity which causes the conduction times for a short series of impulses, each delivered during the supernormal phase left by its predecessor, to show a progressive decrease in length. The second is the appearance during continuous activity of cumulative fatigue, and the recovery from this fatigue which occurs after a minute or two. The author has therefore obtained curves which show, following the post-supernormal depression of conductivity, a gradual return of conductivity with prolonged rest. As a consequence in a typical case a degree of block may often be produced which will cause impulses arriving within 2.5 seconds following a previous impulse to be blocked; from 2.5 seconds to about 7 or 8 seconds, to be transmitted; from 8 to about 25 seconds, to be blocked; and after 25 seconds, to be transmitted. This is a general statement. The success or failure of each individual impulse is also conditioned by the degree of cumulative fatigue or the antecedent appearance of a treppe in conductivity.

The treppe is best seen after an intermediate rest period, i.e., before much recovery from fatigue has occurred. As a consequence of the treppe phenomenon when the compression is right and when a series of impulses at four second intervals arrive after a 20 second rest, the first impulse to be transmitted to the ventricle may be the third, fourth or even the fifth of the series. If the impulses continue to arrive at this rate, several more may be transmitted in succession until a partial block develops as a result of fatigue. The block is ushered in by a prolongation of the

conduction time. If, under these same conditions, a much longer rest is allowed before the series of impulses at four second intervals is delivered at the compressed region, the first impulse may be transmitted most rapidly, the second almost as rapidly, the third somewhat more slowly, the fourth or fifth much more slowly until a partial block develops. Here the treppe is represented, not by a decrease in the A-V interval, but by the failure of the fatigue effects to appear as quickly as they otherwise would.

This relation is perhaps of importance for its bearing upon Iliescu and Sebastiani's criticism of the Kaufmann and Rothberger theory of parasystole (Heart, 1923, x, 101). Iliescu and Sebastiani state that the time relations of the transmission intervals postulated by Kaufmann and Rothberger are not those actually seen in partial block. If a supernormal phase were present, the time relations in question might have been possible.

Book Reviews

STUDIEN ZUM PROBLEM DES PULSUS PARADOXUS.—By L. J. Van der Mandele. Introduction by Prof. Wenckebach. Julius Springer, Vienna, 1925.

This monograph revives interest in a clinical sign the diagnostic value of which has been denied by a great many observers. In a detailed historical summary, the author reviews the subject in its clinical and experimental aspects. Described as early as 1850 by Williams, the paradoxical pulse did not receive widespread attention until the publication of Kussmaul's classical study in 1873. The designation "paradoxical" was applied to this type of pulse by Kussmaul for two reasons: first, though the pulse diminishes in amplitude during inspiration, auscultation reveals no change in the heart action, and secondly, though the pulse is apparently irregular, the changes in the pulse amplitude recur regularly with each respiratory cycle. Kussmaul believed it to be pathognomonic of fibrous mediastinopericarditis, but later observations have shown that it occurs in a large variety of other conditions.

Much confusion has arisen because of failure to define this phenomenon accurately. In pulsus paradoxus there is a periodic waxing and waning of the pulse with each respiration, the pulse becoming smaller or disappearing during inspiration; but the *breathing must not be forced,* and the *cardiac rhythm regular,* i.e., the observed irregularity in the pulse must be one of amplitude only. This rules out at once instances of pulsus paradoxus which develop in healthy individuals after voluntary intensification or acceleration of the breathing as well as cases of sinus arrhythmia of respiratory origin. Among those who consider the paradoxical pulse to be a normal phenomenon, there are many who disregard these criteria.

The author reviews the various theories which have been proposed to explain the paradoxical pulse and gives among others the experiments of Katz and Gauchat (Arch. Int. Med., 1924, xxxiii, 371) in some detail.

In their experiments on dogs, they found that mechanical compression of the aorta produces an immediate effect on the pulse amplitude; compression of the pulmonary veins after one or two beats and compression of the vena cava after three or four beats. These time relations are important to locate the influence of respiration upon the changes in pulse amplitude noted in the paradoxical pulse. Traction anywhere on the pericardium leads to pulsus paradoxus which is proved to be the direct or indirect result of partial occlusion of the pulmonary veins or aorta or both, but not of the vena cava. Experimentally increased oscillations in the intrapleural pressure result in the paradoxical pulse and the more rapidly these fluctuations occur, the more pronounced is the effect on the pulse. Artificially produced pericardial effusions lead to pulsus paradoxus without alteration in the breathing, thus simulating the clinical condition. The time relations show that it is due to the effect of variations in the intrapleural pressure on the volume flow to the left side of the heart.

Employing Wenckebach's classification, the author subdivides the cases of pulsus paradoxus into three types: (a) extrathoracic type, (b) dynamic type, and (c) mechanical type. Pulsus paradoxus extrathoracicus may be found in perfectly healthy persons. It is due to compression of the subclavian artery between the first rib and the clavicle during the inspiratory lift of the thorax and its occurrence is dependent upon special anatomical configurations of the latter. The diminished amplitude of the pulse at the wrist lasts as long as the breath is held in inspiration and disappears at once *if the arm is raised.* This type of paradoxical pulse has no diagnostic significance.

The dynamic type of paradoxical pulse is so designated, because it develops in consequence of the dynamic conditions in the thorax during respiration. Normally, the increase in the negative intrapleural pressure occurring during inspiration does not suffice to affect the venous filling of the heart and the ventricular discharge, but if the extensibility of the lungs is impaired for one reason or another, the changes in the pleural pressure may be great enough to alter the pulse amplitude during respiration. Pulsus paradoxus dynamicus has been observed in the following pathological conditions in each of which the pulmonary extensibility is normal: (1) involuntary acceleration and intensification of the respiration (acidosis dyspnea, moribund state, bronchial asthma, Cheyne-Stokes); (2) stenoses of the upper respiratory passages (croup, laryngitis, tracheal compression, etc.); (3) pathological conditions of the lungs which diminish their extensibility (pneumonia, tuberculosis, pulmonary emphysema); (4) processes which diminish the respiratory space in the thorax (pleural exudates, tumors, pronounced cardiac enlargement, large pericarditic exudates).

The respiratory factor chiefly responsible for pulsus paradoxus in exaggerated breathing is, according to Katz and Gauchat, the rapid fluctuations in the intrapleural pressure. During inspiration the pulmonary veins increase in size, and consequently less blood reaches the heart; whereas during expiration the pulmonary veins decrease in size and more blood reaches the heart. These changes occur normally, but only when the respiration is augmented by the attendant increase in the oscillations of the intrapleural pressure is there sufficient alteration in the ventricular filling (and discharge) to give rise to the paradoxical pulse.

Pulsus paradoxus dynamicus can also develop when the lungs and pleura are healthy and the breathing natural. In such cases the normal intrapleural pressure changes exert an exaggerated influence on the heart and blood vessels. This occurs in: (1) atony of the heart, myocardial degeneration, diminished filling of the heart, etc., also in cardiac debility, dilatation, severe anemia; (2) lowered blood pressure, incomplete filling and anatomical changes in the thoracic aorta, as in anemia, Addison's disease, hypotension, fever, aortitis, etc.; and (3) pericardial effusions.

The dynamic type of pulsus paradoxus, whatever its cause, may be distinguished from the other types of paradoxical pulse by the following characteristics: (a) the pulse waves diminish in amplitude during inspiration; they are smallest at the end of inspiration and greatest during expiration, and during the pause between inspiration and expiration they are of medium size; (b) there is inspiratory collapse of the veins of the neck; and (c) the irregularity of the pulse is increased when the breathing is voluntarily deepened and accelerated.

The mechanical type is the one described by Kussmaul in fibrous mediastinopericarditis and is the most important form of pulsus paradoxus. It is seen in adherent pericardium, synechia between mediastinum and parietal pericardium, other adhesive processes in the thorax, large pericardial effusions, abnormally low position of the diaphragm in pronounced enteroptosis, certain anomalies of the bony wall of the thorax and more rarely other conditions. Its greatest diagnostic value is in the first two of these conditions. The characteristic features of pulsus paradoxus mechanicus are: (a) the sphygmogram has a typical form, viz., the pulse waves become smaller during inspiration and larger during expiration and are largest during the respiratory pause; (b) the periodic waxing and waning of the pulse occurs during natural breathing; and (c) there is no inspiratory collapse of the cervical veins; in fact, there is inspiratory distention of these veins in a certain number of cases.

Failure to define pulsus paradoxus accurately and to differentiate the various types is believed by the author to account for the differences of opinion concerning the diagnostic value of this sign. He does not consider it to be pathognomonic but believes that, if verified graphically, analyzed correctly, and taken in connection with all the clinical findings, the paradoxical pulse is of great value, not only in diagnosis, but as indicated in the case reports in treatment.